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January 31, 2008

VIA FEDEX

Mary C. Till, Esq.  
Office of Patent Legal Administration  
U.S. Patent and Trademark Office  
600 Dulany Street  
MDW  
Room 7D55  
Alexandria, VA 22314

Re: Selected Documents--PTO/FDA Practice Regarding Timeliness of PTE Applications

Dear Ms. Till:

Thank you for taking the time on January 29, 2008, to talk to us.

Further to our telephone discussion, we enclose a binder that contains the documentation for the 14 examples of patent term extension applications that we mentioned to you. In each of these cases, the initial PTO letter to the FDA states that the application was filed on a day that, by our count, corresponds to the 60th day when counting day one as the *day after* the date of FDA approval. For each case, we confirmed that the day preceding the designated filing date was not a Saturday, Sunday or federal holiday. In each case, the PTO granted a certificate of patent term extension. We have included, where available, copies of the PTE application as filed, the initial letter from the PTO to the FDA, the response from the FDA to the PTO indicating timeliness, the Notice of Final Determination and the issued PTE certificate, all separated by blue separator sheets.

January 31, 2008

We greatly appreciate your time and effort in considering this matter.

Best regards,

A handwritten signature in cursive script that reads "Leslie Morioka". The signature is written in dark ink and includes a small circular mark at the end of the last name.

Leslie Morioka

cc: John Genova, Esq.

LM:cc

Enclosure

**Selected Documents--PTO/FDA Practice Regarding Timeliness of PTE Applications**

<b>TAB</b>	<b>PATENT NO.</b>
1.	3,721,687
2.	3,732,340
3.	4,215,113
4.	4,407,288
5.	4,513,006
6.	4,702,253
7.	4,830,010
8.	4,836,217
9.	4,874,794
10.	4,941,093
11.	5,441,745
12.	5,532,221
13.	5,639,639
14.	5,827,937





Paper No. 16

NOTICE

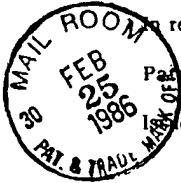
An application for Patent Term Restoration of Patent No. 3,721,687 has been filed under 35 U.S.C. 156 on February 25, 1986.

All papers relating to the Patent Term Restoration application will be retained in the Office of the Director, Group 120 (CP2-9A09; 557-3637) until a final decision on the application is made.

Linda M. Feducia  
Linda M. Feducia  
Secretary, Group 120

#17

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



re United States Patent 3,721,687

Patentee: JOSEPH ELKS ET AL

Attn: Box Patent Ext.

Issue Date: March 20, 1973

LETTER OF TRANSMITTAL OF APPLICATION FOR  
EXTENSION OF PATENT TERM

Honorable Commissioner of  
Patents and Trademark  
Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an application for extension of term of  
U.S. Patent No. 3,721,687 and a duplicate of the papers thereof, certified as  
such.

A check in the amount of \$750.00 to cover the filing fee is enclosed.

The Commissioner is hereby authorized to charge payment of any additional  
fees associated with this communication or credit any overpayment to Deposit  
Account 02-0200. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

BACON & THOMAS

*Richard E. Fichter*  
Richard E. Fichter  
Reg. No. 26,382

February 25, 1986

Suite 300  
1755 Jefferson Davis Hwy  
Arlington, Va. 22202  
(703)979-9340  
REF/dme

02 16/86 372.687

1 111

750.00 CK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent 3,721,687

Patentee: JOSEPH ELKS ET AL

Attn: Box Patent Ext.

Issue Date: March 20, 1973

DUPLICATE OF APPLICATION PAPERS FOR EXTENSION OF  
U.S. PATENT 3,721,687

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

Attached is a duplicate of the application papers for extension of the term  
of U.S. Patent 3,721,687 which application papers are also submitted herewith.

I hereby verify and certify that the attached papers are a duplicate of the original  
application papers for extension of the term of U.S. Patent 3,721,687 and further  
that all statements made herein of my own knowledge are true and that all statements  
made on information and belief are believed to be true; and further that these  
statements were made with the knowledge that willful false statements and  
the like so made are punishable by fine or imprisonment, or both, under Section  
1001 of Title 18 of the United States Code and that such willful false statements  
may jeopardize the validity of the application or any extension of U.S. Patent  
3,721,687.

Date:

February 25, 1986

Richard E. Fichter

Richard E. Fichter  
Reg. No. 26,382  
Agent and Attorney for  
Glaxo Group Limited

BACON & THOMAS  
Suite 300  
1755 Jefferson Davis Hwy  
Arlington, Va. 22202  
(703)979-9340  
REF/dme



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

#18

March 28, 1986

Mr. Ronald Wilson  
Office of the Associate Commissioner  
for Health Affairs (HFY-20)  
Room 11-46  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

RE: Temovate  
FDA Docket # 85E-0097

Dear Mr. Wilson:

Transmitted herewith is a copy of the application for Patent Extension of U. S. Patent No. 3,721,687, issued March 20, 1973. The application was filed on February 25, 1986 under Title II of Public Law 98-417, the Drug Price Competition and Patent Term Restoration Act of 1984.

The patent claims a product that was subject to regulatory review under the Federal Food, Drug and Cosmetic Act. Subject to final review, the subject patent is considered to be eligible for patent term restoration. Thus, a determination of the applicable regulatory review period is necessary. Accordingly, notice and a copy of the application are provided pursuant to 35 USC 156(d)(2)(A).

*C.E. Van Horn*

Charles E. Van Horn  
Director, Group 120  
U. S. Patent and Trademark Office

Richard E. Fichter  
Bacon & Thomas  
Suite 300  
1755 Jefferson Davis Hwy.  
Arlington, VA 22202



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

MAR 24 1986

Re: Temovate  
Docket No. 86E-0097

Mr. Charles E. Van Horn  
Director, Group 120  
U.S. Patent and Trademark Office  
Washington, DC 20231

Dear Mr. Van Horn:

This is in regard to the application for patent extension for U.S. Patent No. 3,721,687, filed by Glaxo Operations UK Limited under 35 U.S.C. § 156. The human drug product claimed by the patent is Temovate, containing clobetasol propionate.

A review of the Food and Drug Administration's official records corroborates that Temovate, the product identified in the patent extension application, was subject to a regulatory review period before its commercial marketing or use as required by 35 U.S.C. § 156(a)(4). FDA reviewed separate new drug applications (NDAs) for two dosage forms (cream and ointment) of Temovate simultaneously. Our records indicate that NDA Nos. 19-322 and 19-323 collectively represent the first permitted commercial marketing or use of the active ingredient, clobetasol propionate, under section 505 of the Federal Food, Drug, and Cosmetic Act. FDA approved both NDAs on December 27, 1985, which makes the submission of the patent term restoration application on February 25, 1986 timely under 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent extension and a determination of the applicable regulatory review period is thus necessary, please advise us. As required by 35 U.S.C. § 156(d)(2)(A), we will then determine the regulatory review period, publish that determination in the Federal Register, and notify you of our determination.

Please let me know if we can provide further assistance.

Sincerely yours,

Ronald L. Wilson  
Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Richard E. Fichter  
Suite 300  
1755 Jefferson Davis Hwy  
Arlington, VA 22202



#22  
UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

November 6, 1986

Richard E. Fichter  
Bacon & Thomas  
Suite 300  
1755 Jefferson Davis Hwy.  
Arlington, VA 22202

RE: Patent Term Extension  
Application for  
U. S. Patent 3,721,687  
Issued March 20, 1973

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 3,721,687, issued March 20, 1973, is eligible for patent term extension under 35 USC 156. The period of extension has been determined to be 2 years.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register on April 28, 1986, as follows:

$$\begin{aligned}\text{Period} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (883) + 485 \\ &= 927 \text{ days}\end{aligned}$$

Since the regulatory review period took place after the patent issue date and there was no determination of a lack of due diligence, the entire period has been considered. The exception of 35 USC 156(c)(3) does not operate to reduce the period determined above. The limitation of 35 USC 156(g)(4)(C) applies in the present situation because Patent No. 3,721,687 was issued (March 20, 1973) before the date of enactment (September 24, 1984) of 35 USC 156; the date of exemption under Section 505(i) of the Federal Food, Drug and Cosmetic Act involving Temovate became effective (April 1, 1982) was before the date of enactment, and the product was not approved for commercial marketing or use (December 27, 1985) before the date of enactment. Since the period of extension calculated under 35 USC 156(c) for Patent No. 3,721,687 and Temovate cannot exceed two (2) years under 35 USC 156(g)(4)(C), the period of extension will be for two (2) years.

A single request for reconsideration of this final determination as to eligibility and the length of extension of the term of U.S. Patent 3,721,687 may be made if filed within one (1) month of the date of this notice. In the absence of such request, the Commissioner will issue to the applicant for extension of the term of Patent No. 3,721,687, a certificate

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. 156

Patent No. : 3,721,687  
Dated : March 20, 1973  
Inventor(s) : Joseph Elks, et al  
Patent Owner : Glaxo Operations  
UK Limited

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

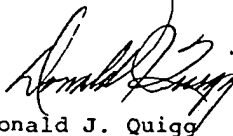
an application under 35 U.S.C. 156 for an extension of the patent term. Since it appears that the requirements of law have been met, this certificate extends the term of the patent for the period of

2 YEARS

with all rights pertaining thereto as provided by 35 USC 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this Nineteenth day of December 1986.

  
Donald J. Quigg

Assistant Secretary and Commissioner  
of Patents and Trademarks

-2-

of extension, under seal, for a period of 2 years. The rights derived from the patent during the period during which the patent is extended are defined in 35 USC 156(b).

C.E. Van Horn

Charles E. Van Horn, Director  
Patent Examining Group 120

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Re: Temovate  
FDA Docket No. 86E-0097



111-550.00-50L  
#9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 3,732,340

Issued: May 8, 1973

To: Herbert ARNOLD, Norbert BROCK  
Friedrich BOURSEAUX and Heinz BEKEL

COPY #1

For: N',O-PROPYLENE PHOSPHORIC  
ACID ESTER DIAMIDES

\* \* \* \* \*

February 28, 1989

SUBMISSION OF APPLICATION FOR EXTENSION OF PATENT TERM UNDER §156

Hon. Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

Submitted herewith are the following papers in support of an application for extension of patent term pursuant to §156 with respect to the subject patent, filed on behalf of Asta-Werke Aktiengesellschaft Chemische Fabrik, a corporation organized under the laws of the Federal Republic of Germany, located in Bielefeld, Federal Republic of Germany, now by change of name, Asta Pharma AG (hereinafter "Applicant"), which is the owner of all right, title and interest in said patent:

- (1) Power of Attorney from ASTA Pharma Aktiengesellschaft to, inter alia, the undersigned. (It should be noted that the Power of Attorney submitted with original Copy #1 of these papers is the originally executed Power of Attorney).
- (2) Application For Extension of Patent Term Under §156 including:

940 01/04/89 3732340

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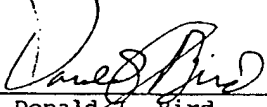
ARNOLD et al  
U.S. Patent No. 3,732,340  
Page 2

- EXHIBIT 1 - Package insert describing the approved product;
  - EXHIBIT 2 - Copy of the subject patent;
  - EXHIBIT 3 - Brief description of significant activities during the applicable regulatory review period.
- (3) Declaration of Donald J. Bird
  - (4) Certificate that these application papers are being submitted in duplicate.
  - (5) Check in the amount of \$550.00, payable to the Commissioner of Patents and Trademarks to cover the prescribed fee.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN

By

  
Donald J. Bird  
Reg. No. 25,323

DJB:sg

1615 L Street, NW  
Eleventh Floor  
Washington, DC 20036-5601

Tel. (202) 861-3027

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 3,732,340

Issued: May 8, 1973

To: Herbert ARNOLD, Norbert BROCK  
Friedrich BOURSEAUX and Heinz BEKEL

For: N',O-PROPYLENE PHOSPHORIC  
ACID ESTER DIAMIDES

\* \* \* \* \*

February 28, 1989

APPLICATION FOR EXTENSION OF PATENT TERM UNDER §156

Hon. Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

ASTA-WERKE AKTIENGESELLSCHAFT CHEMISCHE FABRIK, a corporation organized under the laws of the Federal Republic of Germany, located in Bielefeld, Federal Republic of Germany, now by change of name, Asta Pharma AG (hereinafter "Applicant"), is the owner of the entire interest in and to Letters Patent of U.S. Patent No. 3,732,340 (hereinafter "the Patent") granted to Herbert Arnold, Norbert Brock, Friedrich Bourseaux and Heinz Bekel For N',O-PROPYLENE PHOSPHORIC ACID ESTER DIAMIDES by reason of an assignment to Applicant recorded in the United States Patent and Trademark Office on February 16, 1973 at Reel 2940, Frame 023. BRISTOL-MYERS COMPANY (hereinafter "Bristol-Myers") has been authorized by Applicant to, inter alia, utilize and

distribute the product of the invention claimed in the Patent,  
and to file for and obtain FDA approval for such product.

Applicant, through undersigned counsel, hereby applies  
for a 2 year (731 day) extension of the term of United States  
Patent No. 3,732,340 under 35 U.S.C. §156 on the basis of the  
following information submitted in accordance with the provisions  
of Title 37 C.F.R. §1.740(a)(1)-(17), set forth in the sequence  
of those subparagraphs. Filed herewith is a Power of Attorney  
authorizing the undersigned to file and prosecute this Applica-  
tion for Extension of Patent Term, and to transact all business  
in relation thereto.

(1) This application for extension is based upon the  
regulatory review period before the FDA of Applicant's/Bristol-  
Myers' approved product "IFEX" or sterile ifosfamide, indicated  
for third-line chemotherapy of germ cell testicular cancer.  
"IFEX" or sterile ifosfamide, is a white crystalline powder that  
is administered in a sterile water or other suitable diluent by  
injection or intravenous infusion, as more particularly described  
in the package insert attached hereto as EXHIBIT 1.

(2) The approved product was subject to regulatory  
review under Federal Food, Drug and Cosmetic Act, Section 505 (21  
U.S.C. Section 355).

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U.S. Patent No. 3,732,340  
Page 3

(3) The approved product "IFEX" received permission for commercial marketing or use after a regulatory review period under Section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355) on December 30, 1988.

(4) The active ingredient in the approved product, "IFEX" is ifosfamide. To the best of applicant's knowledge, the permission for the commercial marketing or use of this product after such regulatory review period is the first permitted commercial marketing or use of such product under the Federal Food, Drug and Cosmetic Act.

(5) This application for extension of patent term under 35 U.S.C. §156 is being submitted within the permitted 60 day period, which period will expire on February 28, 1989.

(6) The patent for which an extension is being sought is as follows:

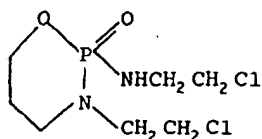
U.S. Patent No. 3,732,340  
Issued: May 8, 1973  
Expires: May 7, 1990  
Inventors: Herbert ARNOLD, Norbert BROCK,  
Friedrich BOURSEAUX and Heinz BEKEL

ARNOLD et al  
U.S. Patent No. 3,732,340  
Page 4

(7) A copy of the patent for which an extension is being sought, including the entire specification, claims and drawings, is attached as EXHIBIT 2.

(8) There is no disclaimer, certificate of correction or reexamination certificate in the subject patent, and it is not subject to maintenance fee payments.

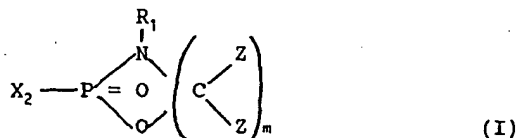
(9) U.S. Patent No. 3,732,340, for which this extension is sought, generally claims a cyclic phosphoric acid derivative of the formula as set forth in claim 1 quoted below. The approved product is sterile ifosfamide as described in Example 4 of the Patent, having the structural formula:



and is covered by each of claims 1, 2, 3, 5 and 6 of the Patent as described in more detail below:

Claim 1:-

A cyclic phosphoric acid derivative of the Formula I:



wherein  $R_1$  is a member selected from the group consisting of the lower alkyl groups having from 1 to 4 carbon atoms and being substituted with a chlorine atom,  $Z$  is a member selected from the group consisting of hydrogen and the lower alkyl groups having from 1 to 4 carbon atoms,  $m$  is a number selected from the group consisting of 2 and 3 and  $X_2$  is a member selected from the group consisting of the ethylene imino group and the group of the Formula II:



in which formula R is a member selected from the group consisting of hydrogen, the lower alkyl groups having from 1 to 4 carbon atoms and being substituted with a chlorine atom and the lower alkyl groups having from 1 to 4 carbon atoms and being substituted with a hydroxy group, and Z and m have the same meaning as given hereinabove.

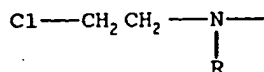
\* \* \* \* \*

The approved product is a cyclic phosphoric acid derivative of Formula I wherein:

R<sub>1</sub> = ClCH<sub>2</sub>CH<sub>2</sub>- = β-chloroethyl  
Z = H-  
m = 3, and  
X<sub>2</sub> = ClCH<sub>2</sub>CH<sub>2</sub>NH-

Claim 2

A cyclic phosphoric acid derivative according to claim 1 wherein X<sub>2</sub> is the group



R<sub>1</sub> is a member selected from the group consisting of the β-chloroethyl and the γ-chloropropyl group, m is 3, and R is a member selected from the group consisting of hydrogen, the methyl group, the ethyl group, the β-chloroethyl group and the β-hydroxy ethyl group.

\* \* \* \* \*



In the approved product:

$X_2 = \text{ClCH}_2\text{CH}_2\text{NH-}$  wherein R in the claim formula is H

$R_1 = \text{ClCH}_2\text{CH}_2- = \beta\text{-chloroethyl}$

$m = 3$

Claim 3

A phosphoric acid derivative according to claim 2,  
wherein  $R_1$  is the  $\beta$ -chloroethyl group.

\* \* \* \* \*

In the approved product,  $R_1$  is  $\text{ClCH}_2\text{CH}_2-$ , which is the  
 $\beta$ -chloroethyl group.

Claim 5

The cyclic phosphoric acid derivative as claimed  
in claim 3, wherein R is hydrogen.

\* \* \* \* \*

In the approved product, R is hydrogen.

Claim 6

The cyclic phosphoric acid derivative as claimed  
in claim 1 wherein Z is hydrogen.

\* \* \* \* \*

In the approved product, Z is hydrogen.

(10) The relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

- (a) Issue date of patent: May 8, 1973
- (b) Effective Date of IND applications:
  - IND # 10,837 - (Ifosfamide)  
filed (received) July 23, 1974  
effective August 22, 1974
  - IND # 16,710 - (Ifosfamide plus N-Acetylcysteine)  
filed (received) August 27, 1979  
effective September 27, 1979
- (c) NDA # 19-763 - submitted December 9, 1987
- (d) NDA # 19-763 - approved December 30, 1988

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U.S. Patent No. 3,732,340  
Page 9

(11) A brief description of the significant activities undertaken by or on behalf of the Applicant during the applicable regulatory review period with respect to the approved product, and the significant dates applicable to such activities, are set out in EXHIBIT 3.

(12) Applicant is of the opinion that U.S. Patent 3,732,340 is eligible for extension under 35 U.S.C. §156 because it satisfies all the requirements for such extension inasmuch as:

- i) such patent claims a product (35 U.S.C. §156(a);
- ii) the term of such patent has not expired before the submission of this application (35 U.S.C. §156(a)(1));
- iii) the term of such patent has never been extended (35 U.S.C. §156(a)(2)),
- iv) the application for extension is submitted by the owner of record, through undersigned counsel, in accordance with the requirements of 35 U.S.C. §156(d);
- v) the approved product, "IFEX" or ifosfamide, has been subject to a regulatory review period before its commercial marketing or use (35 U.S.C. §156(a)(4)); and
- vi) the permission for the commercial marketing or use of the product, "IFEX" or ifosfamide, after the regulatory review period, is the first permitted commercial marketing or use of the approved product under the provisions of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §355) under which such regulatory review period occurred.

Applicant requests an extension of the patent term of U.S. Patent No. 3,732,340 by 2 years (731 days) from the original expiration date of May 7, 1990 to May 7, 1992. This period of extension is calculated according to the following subsections of 37 C.F.R. §1.775:

- (a) The original expiration date of the Patent is 17 years from its date of issue, that is May 7, 1990.
- (c) The length of the regulatory review period was 5244 days, calculated as follows:
  - (1) The number of days from the receipt date of original IND #10,837 for ifosfamide to the submission of NDA #19-763, that is from August 22, 1974 to December 9, 1987 is 4857 days.
  - (2) The number of days between initial submission of the NDA to the approval of the NDA, that is from December 9, 1987 to December 30, 1988, is 387 days.
- (d) The term of the patent as extended for a human drug product is to January 21, 1998, that is an extension of 2816 days, calculated by subtracting 2428 days as follows from the 5244 days of the total regulatory review period from subparagraph (c):

- (1) From the number of days of the regulatory review period calculated under subparagraph (c), the following are subtracted:
  - i) No part of the regulatory review period was before the date on which the patent issued;
  - ii) Applicant believes it acted with diligence in this matter as evidenced by EXHIBIT 3;
  - iii) One half the period defined by paragraph (c)(1), ignoring half days, comes to 2428 days.
- (2) Adding 2816 days to the original expiration date of May 7, 1990 comes to January 21, 1998.
- (3) Adding 14 years to the date of approval of the NDA comes to December 30, 2002.
- (4) The earlier of the dates calculated under subparagraphs (d)(2) and (3) above is January 21, 1998.
- (5) The original patent was not issued after September 24, 1984, so this subparagraph is not applicable.

(6) The original patent was issued before  
September 24, 1984.

i) A request was submitted for an exemption  
(IND) before September 24, 1984, so this  
subparagraph is not applicable.

ii) A request for exemption (IND) was sub-  
mitted before September 24, 1984, and  
the commercial marketing or use of the  
product was not approved before  
September 24, 1984, therefore:

(A) Adding 2 years to the original  
expiration date of the patent comes  
to May 7, 1992;

(B) The earlier of the dates obtained  
pursuant to paragraphs (d)(4) and  
(d)(6)(ii)(A) is May 7, 1992.

(13) Applicant, through its undersigned counsel,  
acknowledges a duty to disclose to the Commissioner of Patents  
and Trademarks and the Secretary of Health and Human Services any  
information which is material to the determination of entitlement  
to the extension sought, in accordance with 37 C.F.R. §1.765.

ARNOLD et al  
U.S. Patent No. 3,732,340  
Page 14

(14) A check in the amount of \$550, payable to the Commissioner of Patents and Trademarks is attached to cover the fee prescribed by 37 C.F.R. §1.20(n) for receiving and acting upon this application for extension. The commissioner is hereby authorized to charge any deficiency, or credit any surplus, in the amount indicated above relative to the required fee to our Account No. 03-3975, Order No. 59808.

(15) Please direct all inquiries and correspondence relating to this application for patent term extension to:

Donald J. Bird  
Cushman, Darby & Cushman  
1615 L Street N.W., 11th Floor  
Washington, D.C. 20036  
(202) 861-3000

(16) Submitted herewith is a certification that these application papers are being submitted in duplicate.



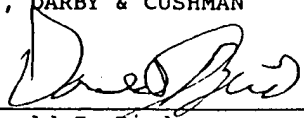
ARNOLD et al  
U.S. Patent No. 3,732,340  
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(17) Additionally submitted herewith is a declaration of Donald J. Bird as patent counsel for Applicant pursuant to 37 C.F.R. §1.740(b)(1) as authorized by the Power of Attorney executed by Applicant submitted herewith.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN

By

  
Donald J. Bird  
Reg. No. 25,323

DJB:sg

1615 L Street, NW  
Eleventh Floor  
Washington, DC 20036-5601

Tel. (202) 861-3027

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 3,732,340

Issued: May 8, 1973

To: Herbert ARNOLD, Norbert BROCK  
Friedrich BOURSEAUX and Heinz BEKEL

For: N',O-PROPYLENE PHOSPHORIC  
ACID ESTER DIAMIDES

\* \* \* \* \*

DECLARATION

To the Commissioner of Patents and Trademarks:

DONALD J. BIRD, as patent counsel for Asta Pharma AG being, by change of name from Asta-Werke Aktiengesellschaft, Chemische Fabrik, the assignee of record of the above-identified patent (hereinafter "Applicant"), declares as follows:

(1) That he is a Registered Patent Attorney and partner with the firm of Cushman, Darby & Cushman, 1615 L Street, 11th Floor, Washington, D.C. 20036, authorized to practice before the United States Patent and Trademark Office under Registration No. 25,323, and that he is authorized by Applicant to file the accompanying APPLICATION FOR EXTENSION OF PATENT TERM UNDER §156, and to execute this Declaration.

(2) That, upon information and belief, Applicant is the assignee of the entire right, title and interest in United States Patent No. 3,732,340 issued May 8, 1973 (hereinafter the "Patent") by reason of an assignment recorded in the United

ARNOLD et al  
U.S. Patent No. 3,732,340  
Page 2

States Patent and Trademark Office on February 16, 1973 at Reel 2940, Frame 023.

(3) That submitted herewith is an Application for Extension of Patent Term Under 35 U.S.C. §156 for the Patent (hereinafter referred to as the "Application") requesting a 2 year (731 day) extension of the term of the Patent.

(4) That he has reviewed and understands the contents of the Application being submitted pursuant to 37 C.F.R. §1.740.

(5) That he believes the Patent is subject to extension pursuant to 37 C.F.R. §1.710.

(6) That he believes an extension of 2 years (731 days) as requested in the Application is justified under 35 U.S.C. §156 and the applicable regulations; and

(7) That he believes the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. §1.720.

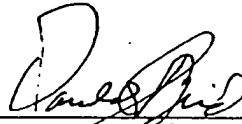
He declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the

ARNOLD et al  
U.S. Patent No. 3,732,340  
Page 3

validity of United States patent 3,732,340, issued May 8, 1973,  
and any extensions thereof.

February 28, 1975

Date




Donald J. Bird  
Reg. No. 25,323

CERTIFICATION

The undersigned hereby certifies that this Application  
For Extension of Patent Term Under 35 U.S.C. § 156, including THE  
EXHIBITS and supporting papers, is being submitted as duplicate  
originals.

February 27, 1989  
Date

  
Donald J. Bird  
Reg. No. 25,323



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

#8

March 6, 1989

Mr. Ronald Wilson  
Health Assessment Policy Staff  
Office of Health Affairs  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Dear Mr. Wilson:

The attached application for patent term extension of U.S. Patent No. 3,732,340, issued May 8, 1973, was filed on February 28, 1989 under Title II of Public Law 98-417.

The assistance of your Office is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC 156(g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 USC 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 USC 156.

C. E. Van Horn

Charles E. Van Horn  
Deputy Solicitor  
U.S. Patent and Trademark Office

Donald J. Bird, Esq.  
Cushman, Darby & Cushman  
1615 L Street, N.W.  
Eleventh Floor  
Washington, D.C. 20036-5601



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

#9

MAR 22 1989

Food and Drug Administration  
Rockville MD 20857

Re: Ifex  
Docket No. 89E-0097

SOLICITOR

MAR 27 1989

U.S. PATENT &  
TRADEMARK OFFICE

Charles E. Van Horn, Esq.  
Deputy Solicitor, Solicitor's Office  
U.S. Patent and Trademark Office  
Washington, DC 20231

Dear Mr. Van Horn:

This is in regard to the application for patent term extension for U.S. Patent No. 3,732,340 filed by Asta Pharma AG under 35 U.S.C. 156. The human drug product claimed by the patent is Ifex (ifosfamide), New Drug Application (NDA 19-763).

A review of the Food and Drug Administration's official records confirms that Ifex was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. 156(a)(4). Our records also indicate that NDA 19-763 represents the first permitted commercial marketing or use of the active ingredient, ifosfamide. The NDA was approved on December 30, 1988 which makes the submission of the patent term extension application on February 28, 1989 timely within 35 U.S.C. 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C 165(d)(2)(A), we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely yours,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)

cc: Donald J. Bird  
Cushman, Darby & Cushman  
1615 L. Street N.W., 11th Floor  
Washington, D.C. 20036



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

#14

OCT 25 1989

Donald J. Bird  
Cushman, Darby & Cushman  
1615 L Street, N.W., 11th Flr.  
Washington, DC 20036

Re: Patent Term Extension  
Application for  
U.S. Patent No. 3,732,340  
Issued May 8, 1973

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 3,732,340, issued May 8, 1973, is eligible for patent term extension under 35 USC 156. The period of extension has been determined to be 2 years.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register on April 12, 1989 as follows:

Period =  $1/2$  (Testing Phase) + Approved Phase  
=  $1/2$  (4859) + 387  
= 2817 days

Since the regulatory review period took place after the patent issue date and there was no determination of a lack of due diligence, the entire period has been considered. The exception of 35 USC 156(c)(3) does not operate to reduce the period determined above. However, the limitation of 35 USC 156(g)(6)(C) applies in the present situation because Patent No. 3,732,340 was issued May 8, 1973 before the date of enactment (September 24, 1984) of 35 USC 156; the date of exemption under Section 505(i) of the Federal Food, Drug and Cosmetic Act involving Ifex became effective (August 26, 1974) was before the date of enactment, and the product was not approved for commercial marketing or use (December 30, 1988) before the date of enactment. Since the period of extension calculated under 35 USC 156(c) for Patent No. 3,732,340 and Ifex cannot exceed two (2) years under 35 USC 156(g)(6)(c), the period of extension will be for two (2) years.

A single request for reconsideration of this final determination as to eligibility and the length of extension of the term of U.S. Patent 3,732,340 may be made if filed within one (1) month of the



date of this notice. This period is not subject to an extension of time under 37 CFR 1.136(a). In the absence of such request, the Commissioner will issue to the applicant for extension of the term of Patent No. 3,732,340 a certificate of extension, under seal, for a period of 2 years. The rights derived from the patent during the period during which the patent is extended are defined in 35 USC 156(b).

Upon issuance of the certificate of extension the following information will be published in the Official Gazette:

U.S. Patent 3,732,340, granted May 8, 1973 to  
Herbert Arnold et al,  
Owner of Record: Asta Pharma AG  
Title: N',O-PROPYLENE PHOSPHORIC ACID ESTER DIAMIDES  
Classification: 558-81  
Product Trade Name: Ifex  
Term Extended: 2 years

*C.E. Van Horn*

Charles E. Van Horn  
Office of the Assistant Commissioner  
for Patents

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

RE: Ifex  
FDA Docket # 39E-0097

#15

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. 156

Patent No. : 3,732,340  
Dated : May 8, 1973  
Inventor(s) : HERBERT ARNOLD ET AL  
Patent Owner : ASTA PHARMA AG

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

2 YEARS

with all rights pertaining thereto as provided by 35 USC 156 (b).



I have caused the seal of the Patent and Trademark Office to be affixed this 11th day of December 1989.

*Jeffrey M. Samuels*

Jeffrey M. Samuels  
Acting Commissioner of  
Patents and Trademarks

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

-----X  
In Re : U.S. Patent 4,215,113

Issued: July 29, 1980

To : Bertil F. H. Eriksson,  
Åke J. E. Helgstrand,  
Alfons Misiorny (deceased-  
legal rep. Karl H. Misiorny)  
Göran B. Stening  
Stig-Åke A. Stridh

For : METHOD FOR COMBATING  
VIRUS INFECTIONS  
-----X

Commissioner of Patents and Trademarks  
Box Patent Extension  
Washington, D.C. 20231

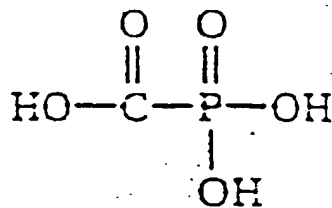
APPLICATION FOR EXTENSION OF  
PATENT TERM UNDER 35 U.S.C. §156

Sir:

Applicant, Aktiebolaget Astra, a corporation organized and existing under the laws of Sweden, whose address is S-151 85 Södertälje, Sweden, represents that it is the assignee of the entire interest in and to letters Patent of the United States No. 4,215,113 granted to Bertil F. H. Eriksson, Åke J.E. Helgstrand, Alfons Misiorny, (deceased - legal representative Karl H. Misiorny), Göran B. Stening, and Stig-Åke A. Stridh on the 29th day of July, 1980 for METHOD FOR COMBATING VIRUS INFECTIONS by virtue of an assignment in favor of Aktiebolaget Astra from Astra Lakemedel Aktiebolag. See "Exhibit A".

Astra Lakemedel Aktiebolag previously held the entire interest in and to United States Letters Patent No. 4,215,113 by virtue of an assignment recorded in the parent application, S/N 807,783 (filed June 20, 1977), on November 4, 1977, Reel 3471/Frames 290-293. Applicant, acting through its duly authorized attorney, hereby submits this application for extension of patent term under 35 U.S.C. §156 by providing the following information required by the rules promulgated by the U.S. Patent and Trademark Office (37 C.F.R. §1.740). For the convenience of the Patent and Trademark Office, the information contained in this application will be presented in a format which will follow the requirements of Section 1.740 of Title 37 of the Code of Federal Regulation.

1. FOSCAVIR® contains as the active ingredient, phosphonoformic acid, whose chemical name is Dihydroxyphosphinecarboxylic acid oxide, in the form of its trisodium salt (trisodium phosphonoformate hexahydrate). Phosphonoformic acid is represented by the following structural formula:



2. The approved product was subject to regulatory review under the Federal Food, Drug and Cosmetic Act Section 505 (21 U.S.C. §355).

3. The approved product, FOSCAVIR®, received permission for commercial marketing or use under section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §355 on September 27, 1991.

4. The only active ingredient in FOSCAVIR® is phosphonoformic acid, which has not been approved for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act prior to the approval of NDA by the Food and Drug Administration on September 27, 1991.

5. This Application for extension of patent term under 35 U.S.C. §156 is being submitted within the permitted 60 day period pursuant to 37 C.F.R. §1.720(f), said period which will expire on November 26, 1991.

6. The complete identification of the patent for which extension is being sought is as follows:

Inventors : Bertil F. H. Eriksson,  
Åke J. E. Helgstrand,  
Alfons Misiorny (deceased-  
legal rep. Karl H. Misiorny)  
Göran B. Stening  
Stig-Åke A. Stridh

Patent Number : 4,215,113

Issued Date : July 29, 1980

Expiration Date: July 29, 1997

7. See "Exhibit B" for a complete copy of the patent identified in paragraph (6) hereof.

8. No disclaimer, certificate of correction, receipt of maintenance fee payment or reexamination certificate has been required or issued with regard to U.S. Patent 4,215,113.

9. U.S. Patent 4,215,113 claims the method of treatment utilizing the active ingredient, phosphonoformic acid, in claims 1-17.

Claim 1 reads as follows:

A method for the selective treatment of virus infections in an animal or human host comprising administering to said host so infected an amount effective to treat said virus infection of phosphonoformic acid or a physiologically acceptable salt thereof.

Claim 2 reads as follows:

A method according to claim 1 for the treatment of infections caused by herpes viruses.

Claim 3 reads as follows:

A method according to claim 1 for the treatment of infections caused by herpes simplex type 1 viruses.

Claim 4 reads as follows:

A method according to claim 1 for the treatment of infections caused by herpes simplex type 2 viruses.

Claim 5 reads as follows:

A method according to claim 1 for the treatment of infections caused by varicella (Herpes zoster) viruses.

Claim 6 reads as follows:

A method according to claim 1 for the treatment of infections caused by cytomegalo viruses.

Claim 7 reads as follows:

A method according to claim 1 for the treatment of infections caused by Epstein-Barr viruses.

Claim 8 reads as follows:

A method according to claim 1 for the treatment of infections caused by influenza viruses.

Claim 9 reads as follows:

A method according to claim 1 for the treatment of infections caused by influenza type A or B viruses.

Claim 10 reads as follows:

A method according to claim 1 for the treatment of infections caused by influenza type A viruses.

Claim 11 reads as follows:

A method according to claim 1 for the treatment of infections, caused by papilloma viruses.

Claim 12 reads as follows:

A method according to claim 1 for the treatment of herpes dermatitis, herpes genitalis, herpes keratitis and herpes encephalitis.

Claim 13 reads as follows:

A method according to claim 1 for the treatment of herpes zoster.

Claim 14 reads as follows:

A method according to claim 1 for the treatment of infectious mononucleosis.



Claim 15 reads as follows:

A method according to claim 1 for the treatment of influenza.

Claim 16 reads as follows:

A method according to claim 1 for the treatment of warts.

Claim 17 reads as follows:

A method according to claim 1, comprising topical administration of phosphonoformic acid or a physiologically acceptable salt thereof.

10. The relevant dates and information pursuant to 35 U.S.C. §156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

(i) Investigational New Drug Application (IND 29,466) for phosphonoformic acid was filed on December 18, 1986 and became effective on January 23, 1987.

(ii) New Drug Application (NDA 20,068) for FOSCAVIR® was initially submitted on April 2, 1990 (subsequent parts were filed on April 25, 1990 and September 18, 1990); and

(iii) New Drug Application (NDA 20,068) for FOSCAVIR® (phosphonoformic acid) was approved on September 27, 1991.

11. As a brief description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period, attached hereto as "Exhibit C" is a chronology of the major communications between the applicant and the FDA from December 18, 1986 and September 27, 1991.

)

12. Applicant is of the opinion that U.S. Patent 4,215,113 is eligible for extension under 35 U.S.C. §156 because it satisfies all of the requirements for such extension as follows:

a. 35 U.S.C. §156(a)

U.S. Patent 4,215,113 claims a method of using a product.

b. 35 U.S.C. §156(a)(1)

The term of the U.S. Patent 4,215,113 has not expired before submission of this application.

c. 35 U.S.C. §156(a)(2)

The term of U.S. Patent 4,215,113 has never been extended.

d. 35 U.S.C. §156(a)(3)

The application for extension is submitted by the owner of record in accordance with the requirement of 35 U.S.C. §156(d) and rules of the U.S. Patent and Trademark Office.

e. 35 U.S.C. §156(a)(4)

The product, FOSSCAVIR®, has been subjected to a regulatory review period before its commercial marketing or use.

f. 35 U.S.C. §156(a)(5)(A)

The commercial marketing or use of the product, FOSCAVIR®, after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §355) under which such regulatory review period occurred.

g. 35 U.S.C. §156(c)(4)

No other patent has been extended for the same regulatory review period for the product, FOSCAVIR®.

13. The length of extension of the patent term of U.S. patent 4,215,113 claimed by applicant is 1126 days or 3.08 years. The length of the extension was determined pursuant to 37 C.F.R. §1.775 as follows:

a. The regulatory review period under 35 U.S.C. §156(g)(1)(B) began on January 23, 1987 and ended on September 27, 1991 which is a total of 1708 days or 4.68 years which is the sum of (i) and (ii) below:

(i) The period of review under 35 U.S.C. §156(g)(2)(B)(i), the "Testing Period", began on January 23, 1987 and ended on April 2, 1990, which is 1165 days or 3.19 years and

(ii) The period of review under 35 U.S.C. §156(g)(2)(B)(ii), the "Application Period", began on April 2, 1990 and ended on September 27, 1991, which is 543 days or 1.49 years;

b. The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in sub-paragraph (13)(a) above (1708 days) less

(i) The number of days in the regulatory review period which were on or before the date on which the patent issued (July 29, 1980) which is zero (0) days [1708 remaining], and

(ii) The number of days during which applicant did not act with due diligence which is zero (0) days [1708 remaining], and

(iii) One-half the number of days determined in sub-paragraph (13)(a)(i) after subtracting (b)(i) and (ii), or 582 days, which leaves 1126 days;

c. The number of days as determined in sub-paragraph (13)(b) (1126 days) when added to the original term of the patent would result in the date, August 28, 2000;

d. Fourteen (14) years when added to the date of NDA approval (September 27, 1991) would result in the date, September 27, 2005;

e. The earlier date as determined in subparagraphs (13)(c) and (13)(d) is August 28, 2000;

f. Since the original patent was issued before September 24, 1984, and no request for exemption was filed until after September 24, 1984, five (5) years when added to the original expiration date of the patent (July 29, 1997) would result in the date, July 29, 2002; and

g. The earlier date as determined in subparagraph (13)(e) and (13)(f) is August 28, 2000.

Therefore, the length of extension of patent term claimed by Applicant is 1126 days or 3.08 years, which is the period of time needed to extend the original expiration of term until August 28, 2000.

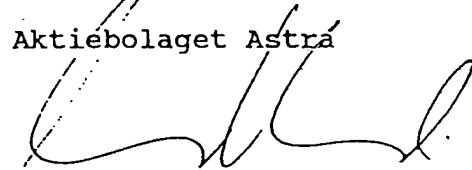
14. Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.

15. The prescribed fee for receiving and acting upon this application is to be charged to the Deposit Account of Applicant as authorized in the attached letter, which is submitted in duplicate. The requisite declaration pursuant to rule 37 C.F.R. 1.740(b) is attached hereto.

Dated: Nov. 26, 1991

Respectfully submitted,

Aktiebolaget Astra

  
Edward V. Filardi  
Reg. No. 25,757

Attorney for Applicant

WHITE & CASE  
1155 Avenue of the Americas  
New York, New York 10036  
(212) 819-8200



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

-----X  
In Re : U.S. Patent 4,215,113 :  
Issued: July 29, 1980 :  
To : Bertil F. H. Eriksson, :  
Åke J. E. Helgstrand, :  
Alfons Misiorny (deceased- :  
legal rep. Karl H. Misiorny) :  
Göran B. Stening :  
Stig-Åke A. Stridh :  
For : METHOD FOR COMBATING :  
VIRUS INFECTIONS :  
-----X

Commissioner of Patents and Trademarks  
Box Patent Extension  
Washington, D.C. 20231

DECLARATION

Sir:

The undersigned Attorney for Aktiebolaget Astra  
(Sweden) which is the Applicant for extension of Patent  
Term under 35 U.S.C. §156 with regard to U.S. Patent No.  
4,215,113 hereby declares as follows:

16. THAT he is a patent attorney authorized to  
practice before the Patent and Trademark Office and has  
general authority from the owner to act on behalf of the  
owner in patent matters;

17. THAT he has reviewed and understands the  
contents of the application being submitted pursuant to 35  
U.S.C. §156 and 37 C.F.R. §1.740;

18. THAT he believes the patent is subject to  
extension pursuant to 35 U.S.C. §156 and 37 C.F.R. §1.710.


19. THAT he believes an extension of the length  
claimed is fully justified under 35 U.S.C. §156.

20. THAT he believes the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 35 U.S.C. §156 and 37 C.F.R. §1.720.

The undersigned hereby declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any extension of patent term issuing thereon.

Further declarant sayeth not.

Singed this 15 day of November, 1991.

  
Edward V. Filardi  
Reg. No. 25,757

Attorney for Applicants

WHITE & CASE  
1155 Avenue of the Americas  
New York, New York 10036  
(212) 819-8200

CERTIFICATION

The undersigned hereby certifies that this application for extension of patent term under 35 U.S.C. 156 including its attachments and supporting papers is being submitted as one original and triplicate copies thereof.

Dated: Mar. 26, 1991

Edward V. Filardi  
Reg. No. 25,757

Attorney for Applicants

WHITE & CASE  
1155 Avenue of the Americas  
New York, New York 10036  
(212) 819-8200



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

DEC 31 1991

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

Dear Mr. Wilson:

The enclosed application for extension of the patent term of U.S. Patent No. 4,215,113 issued on July 29, 1980, was filed on November 26, 1991, under 35 USC § 156.

Your assistance is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC § 156 (g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 USC § 156 (d) (2) (A).

Our review of the application to date indicates that the subject matter would be eligible for extension of the patent term under 35 USC § 156.

*C. E. Van Horn*

---

Charles E. Van Horn  
Patent Policy & Programs Administrator  
Office of the Assistant Commissioner for Patents

cc: Edward V. Filardi  
White & Case  
1155 Avenue of the Americas  
New York, NY 10036



Food and Drug Administration  
Rockville MD 20857

FEB 27 1992

Re: FOSCAVIR  
Docket No. 91E-0026

Charles E. Van Horn  
Patent Policy and Projects Administrator  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

Dear Mr. Van Horn:

This is in regard to the application for patent term extension for U.S. Patent No. 4,215,113 filed by Aktiebolaget Astra under 35 U.S.C. 156. The human drug product claimed by the patent is FOSCAVIR (foscarnet sodium), New Drug Application (NDA) No. 20-068.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the active ingredient, foscarnet sodium.

The NDA was approved on September 27, 1991, which makes the submission of the patent term extension application on November 26, 1991, timely within the meaning of 35 U.S.C. 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Edward V. Filardi  
White & Case  
1155 Avenue of the Americas  
New York, NY 10036

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

PATENT NO.: 4,215,113  
DATED: July 29, 1980  
INVENTORS: Bertil F. H. Eriksson et al.  
PATENT OWNER: Aktiebolaget Astra

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

1,042 DAYS

with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 20th day of May 1993.

*Michael K. Kirk*

Michael K. Kirk  
Acting Commissioner of Patents and Trademarks

#10

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Patent of )

ALOIS A. LANGER, )  
STEVE A. KOLENIK, )  
MARLIN S. HEILMAN, )  
MIECZYSLAW MIROWSKI and )  
MORTON M. MOWER )

Patent No.: 4,407,288  
Issued: October 4, 1983  
Assignee: Mieczyslaw Mirowski

For: IMPLANTABLE HEART STIMULATOR )  
AND STIMULATION METHOD )

Application for Patent Term Extension Under 35 USC §156 and 37 CFR §1.740

Commissioner of Patents and Trademarks  
Box Patent Ext.  
Washington, DC 20231

Dear Sir:

RECEIVED  
AUG 16 1994  
SPECIAL PROGRAMS OFFICE  
A/C PATENTS

Please extend the term of US Patent 4,407,288 under 35 USC §156 by a total of 1107 days. The following information, numbered according to like numbered sub-sections of 37 CFR §1.740(a), supports this request.

(1) The Approved Product

The approved product is the CPI® Ventak® PRx® AICD™ System, an implantable cardioverter defibrillator and ventricular pacing system manufactured by Cardiac Pacemakers, Inc. (CPI). The system primarily comprises an implantable Ventak® PRx® Model 1700 or Model 1705 Pulse Generator, an external Prescriptor® System (programmer) Model 2850, and a Program Disk (programmer software) Model 2860. (The system is designed for use with a variety of cardiac leads along with ancillary accessories such as lead adapters, wrenches, magnets, electrical cables, etc., none of which were subject to the specific regulatory review at issue.) The system detects and terminates ventricular tachycardia and ventricular fibrillation, and provides pacing for bradycardia.

The pulse generators are multimodal treatment systems for patients with serious or potentially serious ventricular arrhythmias. In addition to delivering shocks for terminating malignant arrhythmias, a wide variety of antitachycardia pacing schemes are available to terminate slower, more stable ventricular tachyarrhythmias. Bradycardia pacing is available for bradycardia as well as to support the cardiac rhythm after defibrillation shock therapy.

Programmable parameter settings allow incremental adjustment of therapy to meet patient needs.

The Model 1700 and 1705 Pulse Generators differ slightly in volume and weight due primarily to different connection ports for the electrode leads. Specifically, the Model 1700 Pulse Generator has two 3.2mm morphology/defibrillation lead ports and one 3.2mm inline bipolar rate-sensing/pacing lead port. The Model 1705 Pulse Generator has two 6.1mm morphology/defibrillation lead ports and two 4.75mm rate-sensing/pacing lead ports. These differences are not relevant to the reading of the claims of US Patent 4,407,288 on either model of pulse generator, and thus both models are considered to be one product for purposes of regulatory review under the FFDCA as well as the scope and term of US Patent 4,407,288.

The Prescriptor<sup>®</sup> System Model 2850 programmer system, when loaded with software from the Program Disk Model 2860, communicates with the Ventak<sup>®</sup> PRx<sup>®</sup> Model 1700 and Model 1705 Pulse Generators to: program therapy parameters for the implanted pulse generator; interrogate the programmed pulse generator; monitor and analyze patient data, and evaluate alternative prescription modes; store patient data that can be recalled later for analysis; generate printed reports that detail pulse generator functions, stored patient data, and test results; and perform noninvasive diagnostic tests in an electrophysiology laboratory, operating room, emergency room, or at a patient's bedside.

(2) The Federal Statute under which Regulatory Review Occurred

The US Food and Drug Administration (FDA) reviewed the CPI<sup>®</sup> Ventak<sup>®</sup> AICD<sup>™</sup> System under Section 515 of the Federal Food, Drug and Cosmetic Act (FFDCA).

(3) The Date on which the Product Received Permission for Commercial Marketing

The FDA approved the CPI<sup>®</sup> Ventak<sup>®</sup> AICD<sup>™</sup> System under Section 515 of the FFDCA on June 17, 1994.

(4) The Active Ingredient of a Drug Product

Not applicable.

(5) Timely Filing of this Application

This application is being submitted within the sixty day period set forth in 37 CFR §1.720(f). The product was approved for commercial marketing on Friday, June 17, 1994, the 168th day of



1994. The last date on which this application could be filed is Tuesday, August 16, 1994, the 228th (168+60) day of 1994.

(6) **The Patent**

US Patent 4,407,288 issued October 4, 1983 in the names of Alois A. Langer, Steve A. Kolenik, Marlin S. Heilman, Mieczyslaw Mirowski, and Morton M. Mower. The expiration date of the patent is October 4, 2000.

(7) **Copy of the Patent**

A full copy of US Patent 4,407,288 is enclosed.

(8) **Disclaimers/Corrections/Maintenance Fee Receipts**

No disclaimer of the patent has been filed. No certificate of correction to the patent has been filed. Copies of the Maintenance Fee Receipts for each of the two maintenance fees which have been paid to date are enclosed. No reexamination certificate has been issued for the patent.

(9) **The Approved Product and the Patent**

US Patent 4,407,288 claims the Ventak® PRx® AICD™ System, and the method of using the system, in at least the claims specifically identified below.

**Claim 1** The Ventak® PRx® AICD™ System employs an implantable pulse generator to provide electrical stimulation to the heart. The pulse generator can detect the presence of multiple arrhythmias, and may be programmed to treat any single arrhythmia or multiple arrhythmias. The system determines cardiac condition and selects a unique mode of operation corresponding to the arrhythmia (and preprogrammed command parameters specific to the arrhythmia). The system then administers the appropriate therapy for the condition detected.

**Claim 2** The Ventak® PRx® AICD™ System detects bradycardia, ventricular tachyarrhythmia, and ventricular fibrillation. It provides pacing for bradycardia, anti-tachycardia pacing, and shock therapy for cardioversion or defibrillation. The Ventak® PRx® AICD™ system operates continuously to monitor and treat those conditions.

**Claim 3** The Ventak® PRx® AICD™ System provides cardiac pacing for bradycardia

or post-shock bradycardia as one mode of operation.

- Claim 4** The Ventak® PRx® AICD™ System provides cardiac shocks for cardioversion of ventricular tachycardia as one mode of operation.
- Claim 5** The Ventak® PRx® AICD™ System provides cardiac shocks for ventricular defibrillation as one mode of operation.
- Claim 7** The Ventak® PRx® Model 1700 and Model 1705 Pulse Generators are microprocessor-controlled systems, programmed externally from the Prescriptor® Model 2850 System (using the Program Disk Model 2860) with respect to a variety of bradycardia, cardioversion, and defibrillation parameters.
- Claim 10** See claim 1 above.
- Claim 11** See claim 2 above.
- Claim 12** See claim 3 above.
- Claim 13** See claim 4 above.
- Claim 14** See claim 5 above.
- Claim 18** The Ventak® PRx® Model 1700 and Model 1705 Pulse Generators employ programmable memory registers to store definitional and operating parameters corresponding to the multiple modes of operation. Data is transferred into and out of the registers under the microprocessor direction by means of an input/output data channel. The data values are used by the system to deliver therapy specifically tailored to the arrhythmic condition of the patient.
- Claim 19** See claim 18 above. Also, the Ventak® PRx® System provides for increasing cardioversion/defibrillation energy levels as described for claim 31, below.
- Claim 20** See claims 1 and 10 above.
- Claim 22** The Ventak® PRx® Model 1700 and Model 1705 Pulse Generators have data input/output capability for exchanging data with the Prescriptor® System Model 2850.

- Claim 23** See claims 1 and 18 above.
- Claim 24** See claim 3 above.
- Claim 25** See claim 4 above.
- Claim 26** See claim 5 above.
- Claim 29** See claims 1 and 22 above.
- Claim 30** Pacing pulse amplitude is programmable at 2.5, 5.0, or 7.5 volt (nominal=7.5V); first and second shock cardioversion/defibrillation energy is programmable at 0.10, 0.25, 0.50, and 0.75 joule, 1-10 joule in 1 joule increments, 10-20 joule in 2 joule increments, 25, 30, or 34 joule (nominal=34J).
- Claim 31** In a given episode of cardioversion/defibrillation therapy, up to five shocks may be delivered by the system. The first and second shock energies are programmable as described in claim 30, above; the third, fourth, and fifth energies are fixed at 34 joules. Thus, the system can be programmed to provide a sequence of successive shocks of increasing energy level until defibrillation is completed.
- Claim 32** The system may be preprogrammed to provide 0 or 5 (nominal=5) defibrillating pulses in each episode of antitachycardia therapy.
- Claim 33** See claim 32 above.
- Claim 36** See claims 1 and 22 above.
- Claim 37** See claims 1 and 18 above.

**(10) Relevant Dates and Other Information**

The holder of the regulatory approval for the CPI® Ventak® AICD™ System is Cardiac Pacemakers, Inc. (CPI), a wholly-owned subsidiary of Eli Lilly and Company, exclusive licensee of US Patent 4,407,288.

Under 37 CFR §1.740(a)(10)(v), the following events and dates are applicable to the regulatory review and approval sought and granted to CPI for the Ventak® AICD™ System. (37 CFR §1.740(a)(10)(i-iv) are not applicable.)

Effective Date of Investigational Device Exemption (IDE): November 21, 1990  
(Please note that this is the date that the IDE was conditionally accepted.)

IDE Number: G900150

Date of Pre-Market Approval Application (PMAA): December 20, 1991

Number of PMAA: P910077

Date of Approval of PMAA: June 17, 1994

(11) Significant Activities

A partial listing of key events and mailing dates of correspondence between Cardiac Pacemakers, Inc. and the Food and Drug Administration (FDA) during the regulatory review period appears below. The number and frequency of events clearly establishes that, during the entire regulatory review period, Cardiac Pacemakers, Inc. continuously and diligently pursued approval by the FDA under the FDCA to commercially distribute the CPI® Ventak® PRx® AICD™ System.

Investigational Device Exemption (IDE) Phase

Application	July 25, 1990
Disapproval	August 24, 1990
First Amendment	September 11, 1990
Disapproval of Amended IDE	October 11, 1990
Second Amendment	October 22, 1990
Conditional Approval	November 21, 1990
Submission of Additional Information	November 29, 1990
Supplement	December 18, 1990
Submission of Additional Information	December 18, 1990
Supplement	December 18, 1990
Supplement	January 17, 1991
Continued Conditional Approval	January 18, 1991
Approval of Supplement	January 18, 1991
Conditional Approval of Supplement	February 21, 1991
Supplement	March 5, 1991
Amendment	March 5, 1991
Supplement	March 8, 1991
Approval of Supplement	March 28, 1991
Approval of IDE Application	March 28, 1991
Approval of Supplement	April 10, 1991
Supplement	April 23, 1991
Approval of Supplement	May 2, 1991
Supplement	July 29, 1991
Supplement	August 2, 1991
Approval of Supplement	August 12, 1991

Investigational Device Exemption (IDE) Phase, continued

Approval of Supplement	August 20, 1991
Supplement	September 6, 1991
Supplement	September 16, 1991
Questions Regarding Pre-Market Approval Application	September 30, 1991
Supplement	October 8, 1991
Approval of Supplement	October 9, 1991
Approval of Supplement	October 16, 1991
Response to Questions	October 25, 1991
Approval of Supplement	November 4, 1991
Submission of Data	November 11, 1991
Confirmation of Meeting to Review Data	November 13, 1991
Approval of Supplement	January 2, 1992
Approval of Supplement	January 2, 1992
Supplement	January 10, 1992
Approval of Supplement	February 12, 1992
Approval of Supplement	February 14, 1992
Supplement	March 27, 1992
Approval of Supplement	April 30, 1992
Approval of Supplement	April 30, 1992
Supplement	May 1, 1992
Supplement	May 12, 1992
Supplement	May 13, 1992
Conditional Approval of Supplement	June 3, 1992
Approval of Supplement	June 3, 1992
Disapproval of Supplement	June 11, 1992
Correction of Disapproval of Supplement	June 19, 1992
Request for Modification	July 7, 1992
Supplement	July 20, 1992
Approval of Supplement	August 11, 1992
Confirmation of Telephone Conversation	August 20, 1992
Supplement	August 21, 1992
Confirmation of Telephone Conversation	September 1, 1992
Supplement	September 8, 1992
Supplement	September 17, 1992
Conditional Approval of Two Supplements	September 24, 1992

Investigational Device Exemption (IDE) Phase, continued

Disapproval of Supplement	October 13, 1992
Supplement	October 16, 1992
Conditional Approval of Supplement	November 19, 1992
Supplement	December 23, 1992
Supplement	January 7, 1993
Response to Conditional Approval of Supplement	January 7, 1993
Conditional Approval of Supplement	January 22, 1993
Approval of Supplement	January 29, 1993
Approval of Supplement	January 29, 1993
Supplement	February 9, 1993
Supplement	February 8, 1993
Response to Conditional Approval of Supplement	March 4, 1993
Approval of Supplement	March 11, 1993
Approval of Supplement	March 19, 1993
Supplement	March 31, 1993
Approval of Supplement	April 2, 1993
Supplement	April 13, 1993
Confirmation of Telephone Conversations	April 29, 1993
Conditional Approval of Supplement	April 30, 1993
Supplement	May 3, 1993
Disapproval of Supplement	May 12, 1993
Supplement	May 14, 1993
Response to Questions	June 1, 1993
Approval of Supplement	June 3, 1993
Supplement	June 11, 1993
Approval of Two Supplements	June 17, 1993
Supplement	June 28, 1993
Approval of Supplement	June 30, 1993
Approval of Supplement	July 14, 1993
Supplement	July 15, 1993
Approval of Supplement	July 29, 1993
Conditional Approval of Supplement	August 13, 1993
Supplement	September 13, 1993
Supplement	October 8, 1993
Approval of Supplement	October 14, 1993

Investigational Device Exemption (IDE) Phase, continued

Supplement	October 26, 1993
Conditional Approval of Supplement	November 26, 1993
Supplement	December 6, 1993
Approval of Supplement	January 6, 1994
Supplement	February 22, 1994

Pre-Market Approval Application (PMAA) Phase

Application	December 20, 1991
Threshold Determination	February 14, 1992
Notice of Deficiencies	March 5, 1992
Notice of Deficiencies	May 5, 1992
Amendment	August 1, 1992
Amendment	August 5, 1992
Amendment	October 7, 1992
Amendment	February 11, 1993
Amendment	February 25, 1993
Amendment	March 8, 1993
Notice of Deficiencies	June 7, 1993
Amendment	June 25, 1993
Response to Questions	June 29, 1993
Amendment	July 7, 1993
Notice of Panel Meeting	July 7, 1993
Amendment	July 12, 1993
Amendment	August 19, 1993
Notice of Deficiencies	October 25, 1993
Amendment	November 11, 1993
Amendment	December 6, 1993
Amendment	December 7, 1993
Submission of Additional Copies of November 11, 1993 Amendment	March 10, 1994
Notice of Approvable PMAA	April 29, 1994
Amendment	May 6, 1994
Amendment	June 10, 1994
Submission of Summary of Safety and Effectiveness	June 16, 1994
Approval of PMAA	June 17, 1994
Submission of Amended Labeling	June 20, 1994



**(12) Eligibility for and Calculation of Extension**

In the opinion of the Estate of Mieczyslaw Mirowski, US Patent 4,407,288 is eligible for an extension of patent term under 35 USC §156 in the amount of 1107 days, as set forth below.

**(a) Eligibility for extension under 35 USC §156**

- (1) This application is being submitted prior to the expiration of US Patent 4,407,288 on October 4, 2000.
- (2) US Patent 4,407,288 has never had an extension of patent term.
- (3) This application is being submitted on behalf of the Estate of Mieczyslaw Mirowski, now deceased, the assignee of record. Proof of authority to submit this application, in accordance with 35 USC §156(d) and 37 CFR §1.740(b)(1), will be provided in response to an order to show cause why the USPTO should not deny this application under 35 USC §156(c)(3) and 37 CFR §1.730; or by way of petition under 37 CFR §1.181, §1.182, or §1.183, all as provided by 37 CFR §1.740(c).
- (4) The product was subject to regulatory review by the US Food and Drug Administration (FDA) under Section 515 of the Federal Food, Drug and Cosmetic Act (FFDCA).
- (5) The permission for commercial marketing under Section 515 of the FFDCA was the first permission for commercial marketing for the product.

**(b) Calculation of Length of Extension**

The period beginning on the date a clinical investigation on humans involving the product was begun, i.e., the date the Application for Investigational Device Exemption (IDE) was conditionally accepted (November 21, 1990), and ending on the date the Pre-Market Approval Application (PMAA) was filed (December 20, 1991), is 394 days.

The period beginning on the date the PMAA was filed (December 20, 1991), and ending on the date the product was approved for commercial marketing (June 17, 1994), is 910 days (taking the leap day of February 29, 1992 into account).

The sum of the two periods above is 1304 days. US Patent 4,407,288 issued on October 4,

1983, before the September 24, 1984 date of enactment, as defined in 35 USC §(f)(7), of the statute now codified at 35 USC §156. None of the events described in 35 USC §156(g)(6)(B) (i-iii) occurred. Thus, no reduction under 35 USC 156(g)(3)(B) applies, and the total regulatory review period is 1304 days.

US Patent 4,407,288 issued on October 4, 1983, before clinical investigation on humans involving the product began on December 20, 1991, and thus the regulatory review period is not reduced under 35 USC §156(c).

Cardiac Pacemakers, Inc. continuously and diligently worked to secure acceptance of the PMAA by the FDA during the entire period of regulatory review. Therefore, no reduction for lack of diligence should be made under 35 USC §156 (c)(1) or 37 CFR §1.777(d)(1)(ii).

One-half of the period beginning on the date the IDE was conditionally accepted (November 21, 1990), and ending on the date the PMAA was filed (December 20, 1991), is one-half of 394 days, or 197 days. Under 35 USC §156 (c)(2), this amount is subtracted from the length of the regulatory review period. The difference is 1304 days minus 197 days, or 1107 days.

As of the date of commercial approval of the product, June 17, 1994, the patent term remaining (to October 4, 2000) was 2301 days (6.3 years). The sum of this amount and the reduced regulatory period of 1107 days (3.0 years), is 9.3 years, less than the maximum 14 year (5110 days) extended term permitted by 35 USC §156(c)(3) and 37 CFR §1.777(d)(2-4). Thus, the reduced regulatory period is not reduced further to provide a maximum extended term of not greater than 14 years.

US Patent 4,407,288 issued before, but clinical evaluation of the product began after, September 24, 1984. Because commercial marketing of the product also was approved after that date, the maximum amount of extension available is 5 years. The reduced regulatory period of 3.0 years does not exceed this amount. Thus, the limitation of 35 USC §156(g)(4)(B) and 37 CFR §1.777(d)(6) does not apply.

Therefore, US Patent 4,407,288 is eligible for an extension of term of 1107 days. The new expiration date of the patent should be October 16, 2003.

**(13) Duty of Disclosure**

I acknowledge my duty to disclose to the Commissioner of Patents and Trademarks and the

Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension of patent term of US Patent 4,407,288. I specifically acknowledge the requirements of 37 CFR §1.765.

In this regard, please note two particular issues:

- (1) Extensions of patent term have been previously granted for patents which may also read on the CPI® Ventak® PRx® AICD™ System; and US Patent 4,407,288 may also read on other products which have undergone regulatory review such that other patents on such other products were granted extensions of term.

Specifically, patent term extensions have been granted previously for:

- US Patent B1 Re. 27,757 (a reissue of US Patent 3,614,955, as reflected by Reexamination Certificate Number 638 issued March 10, 1987), based upon regulatory review of implantable defibrillators known as the AID® Model B and AID® Model BR; this patent (now expired) is believed to read on the CPI® Ventak® PRx® AICD™ System. US Patent 4,407,288 is not believed to read on the AID® Model B or Model BR.
- US Patent 4,316,472, based upon regulatory review of an implantable cardioverter defibrillator known as Ventak® P Model 1600, certain claims of which patent also read on certain implantable cardioverter/defibrillators which did not require regulatory review as defined by 35 USC §156(g), specifically those known as Ventak® Model 1550 and Ventak® Model 1555; this patent is believed to read on the Ventak® PRx® Models 1700 and 1705. Certain claims of US Patent 4,407,288 may read on the Ventak® P Model 1600, the Ventak® Model 1550, and the Ventak® Model 1555, depending upon factual issues regarding interpretation of the claims.
- US Patent 4,868,908, based on regulatory review of an implantable cardioverter defibrillator pacer known as Ventritex® Cadence® Tiered Therapy Defibrillator System Model V-100; it is not known if this patent reads on the CPI® Ventak® PRx® AICD™ System. US Patent 4,407,288 is believed to read on the Ventritex® Cadence® Tiered

Therapy Defibrillator System Model V-100.

- US Patent 4,052,991, based upon an implantable cardioverter defibrillator pacer known as Medtronic® PCD® Tachyarrhythmia Control Device Model 7217B; this patent is believed to read on the CPI® Ventak® PRx® AICD™ System. US Patent 4,407,288 is believed to read on the Medtronic® PCD® Tachyarrhythmia Control Device Model 7217B.

- (2) Mr. Gerald Dost of the USPTO and I discussed the eligibility of US 4,407,288 for patent term extension on July 6, 1994. The specific context discussed was the second bullet item above, i.e., that some of the claims of US 4,407,288 may read on at least the CPI® Ventak® P Model 1600, and some of the claims of US 4,316,472 read on the CPI® Ventak® PRx® AICD™ System.

On these facts, 37 CFR §1.720(e)(1) appears to prohibit extension of the term of US Patent 4,407,288 if the "commercial marketing or use" identified in the regulation is read to mean the commercial marketing or use of *any product* which had undergone regulatory review forming the basis for *any* extension, even if such extension was not for US Patent 4,407,288. However, Mr. Dost indicated that 37 CFR §1.720(e)(1) did not prohibit approval of this application, based on the facts as presented in the telephone conversations. I understand that Mr. Dost's interpretation of 37 CFR §1.720(e)(1) was informal and does not substitute for formal review of this application.

(14) Fee

As noted in the letter of transmittal, please charge the \$1,000 fee under 37 CFR §1.20(j) to Deposit Account 03-0667. Please also charge any other fee necessary to process this application to Deposit Account 03-0667.

**(15) Notice**

Please address all inquiries and correspondence regarding this application to:

Peter Forrest  
Mail Stop A390  
Cardiac Pacemakers, Inc.  
4100 Hamline Avenue North  
St. Paul, MN 55112-5798

Please address all telephone calls to Peter Forrest at (612) 582-4400.

**(16) Duplicate Papers**

Please find enclosed one original and four complete duplicates of this application and all exhibits. One duplicate is required by 37 CFR §1.740(a)(16), and three additional duplicates provided for the convenience of the USPTO at the request of Mr. Dost. I certify as a registered practitioner that all duplicates are true and accurate photocopies of the original.

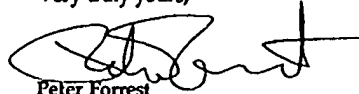
**(17) Declaration**

I am an attorney authorized to practice before the United States Patent and Trademark Office. I have reviewed and I understand the contents of this application. I believe that US Patent 4,407,288 is subject to extension pursuant to 37 CFR §1.710. I believe that an extension of 1107 days is justified under 35 USC §156 and applicable regulations. I believe that US patent 4,407,288 meets the conditions for extension of term as set forth in 37 CFR §1.720.

All statements in this application made of my own knowledge are true, and all statements in this application made on information and belief I believe to be true. I make these statements knowing that willful false statements and the like may be punished by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may also jeopardize this application for extension of the patent term of US Patent 4,407,288.

If you have any questions, please contact me at your convenience.

Very truly yours,



Peter Forrest  
Registration Number 33,235

August 15, 1994

CARDIAC PACEMAKERS, INC.  
Mail Stop A390  
4100 Hamline Avenue North  
St. Paul, MN 55112-5798 USA  
1-800-CARDIAC, ext. 4400 (voice)  
(612) 582-4400 (direct voice)  
(612) 582-2926 (facsimile)



#12  
**UNITED STATES DEPARTMENT OF COMMERCE**  
**Patent and Trademark Office**  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

AUG 22 1994

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

Dear Mr. Wilson:

The enclosed application for extension of the patent term of U.S. Patent No. 4,407,288 issued on October 4, 1983, was filed on August 16, 1994, under 35 USC § 156.

Your assistance is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC § 156(g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 USC § 156(d)(2)(A).

Our review of the application to date indicates that the subject matter would be eligible for extension of the patent term under 35 USC § 156. However, in view of the noted death of the inventor-assignee, it is apparent that Peter Forrest, the registered patent attorney who filed the application for patent term extension on behalf of the licensee-marketing applicant, did not have authorization to act on behalf of the beneficial owner of the patent, the Estate of Mieczyslaw Mirowski, at the time the application for patent term extension was filed.

*C. E. Van Horn*

Charles E. Van Horn  
Deputy Assistant Commissioner  
for Patent Policy and Projects

cc: Peter Forrest  
Mail Stop A390  
Cardiac Pacemakers, Inc.  
4100 Hamline Avenue North  
St. Paul, MN 55112-5798



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

#14

SEP 21 1994

Food and Drug Administration  
Rockville MD 20857

Re: CPI® Ventak® PRx® AICD™ System  
SEP 23 AM 11:23  
Docket No. 94E-0315  
COMMISSIONER FOR PATENTS

Charles E. Van Horn  
Deputy Assistant Commissioner for  
Patent Policy and Projects  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

Dear Mr. Van Horn:

This is in regard to the application for patent term extension for U.S. Patent No. 4,407,288 filed by Cardiac Pacemakers, Inc., under 35 U.S.C. § 156. The medical device claimed by the patent is CPI® Ventak® PRx® AICD™ System, which was assigned Premarket Application (PMA) number P910077.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of this product under section 515(d) of the Federal Food, Drug, and Cosmetic Act.

The PMA was approved on June 17, 1994, which makes the submission of the patent term extension application on August 16, 1994, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A), we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Peter Forrest  
Mail Stop A390  
Cardiac Pacemakers, Inc.  
4100 Hamline Avenue North  
St. Paul, MN 55112-5798





UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

#21

AUG 22 1995

Peter Forrest  
Mail Stop A390  
Cardiac Pacemakers, Inc.  
4100 Hamline Ave. North  
St. Paul, MN 55112-5798

Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,407,288

### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,407,288, which claims the medical device CPI VENTAK PRx AICD System (an implantable cardioverter defibrillator and ventriculator pacing system), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 1107 days.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of November 15, 1994. Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= 1/2 \text{ (Testing Phase) + Approval Phase} \\ &= 1/2 (398 - 0) + 908 \\ &= 1107 \text{ days}\end{aligned}$$

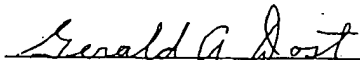
Since the regulatory review period began November 21, 1990, after the patent issue date (October 4, 1983), the entire period has been considered in the above determination. No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The 14 year exception of 35 U.S.C. § 156(c)(3) and the limitations of 35 U.S.C. § 156(g)(6) do not operate to further reduce the period of extension determined above.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Commissioner will issue a certificate of extension, under seal, for a period of 1107 days.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.:	4,407,288
Granted:	October 4, 1983
Applicant:	Alois A. Langer et al.
Owner of Record:	Mieczyslaw Mirowski
Title:	IMPLANTABLE HEART STIMULATOR AND STIMULATION METHOD
Classification:	607/4
Product Trade Name:	CPI VENTAK PRx AICD System
Term Extended:	1107 days

  
Gerald A. Dost  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

(703) 305-9285

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

RE: CPI VENTAK PRx AICD System  
FDA Docket No.: 94E-0315

#2:

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

PATENT NO. : 4,407,288  
DATED : October 4, 1983  
INVENTOR(S) : Alois A. Langer et al.  
PATENT OWNER : Mieczyslaw Mirowski

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

1,107 DAYS

from the original expiration date of the patent, December 11, 2000, subject to the requirements of 35 U.S.C. § 41, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).




I have caused the seal of the Patent and Trademark Office to be affixed this 25th day of April 1996.

*Bruce A. Lehman*

Bruce A. Lehman  
Assistant Secretary of Commerce and  
Commissioner of Patents and Trademarks

Respectfully submitted,

By 

John R. Crossan  
Reg. No. 27,433,  
ATTORNEY FOR APPLICANT

CHAPMAN AND CUTLER  
111 West Monroe Street  
Chicago, Illinois 60625  
(312) 845-3000

NOV - 5 1998



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 15-22  
Rockville, MD 20857

49

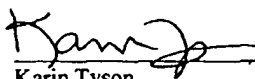
Dear Mr. Wilson:

The attached application for patent term extension of U.S. Patent No. 4,513,006 was filed on February 24, 1997 (certificate of mailing February 20, 1997), under 35 U.S.C. § 156, and supplemented on November 3, 1998.

The assistance of your Office is requested in confirming that the product identified in the application, TOPAMAX®, has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156.

Inquiries regarding this communication should be directed to the undersigned at (703) 306-3159 (telephone) or (703)308-6916 (facsimile).

  
Karin Tyson  
Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

cc: AUDLEY A. CIMPORCERO, JR.  
ONE JOHNSON PLAZA  
NEW BRUNSWICK NJ 08933-7003

kt



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Rockville MD 20857

MAY 2 2001

#10

Re: Topamax  
Docket No. 98E-1217

The Honorable Q. Todd Dickinson  
Director of U.S. Patent and Trademark Office  
Commissioner for Patents  
Box Pat. Ext.  
Washington, D.C. 20231

Dear Director Dickinson:

This is in regard to the application for patent term extension for U.S. Patent No. 4,513,006 filed by McNeilab, Inc. under 35 U.S.C. § 156. The human drug product claimed by the patent is Topamax (topiramate), which was assigned new drug application (NDA) No. 20-505.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in *Glaxo Operations UK Ltd. v. Quigg*, 706 F. Supp. 1224 (E.D. Va. 1989), *aff'd*, 894 F. 2d 392 (Fed. Cir. 1990).

The NDA was approved on December 24, 1996, which makes the submission of the patent term extension application on February 24, 1997, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the *Federal Register*, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely yours,

Jane A. Axelrad  
Associate Director for Policy  
Center for Drug Evaluation and Research

cc: Audley A Ciporcero, Jr.  
One Johnson and Johnson Plaza  
New Brunswick, NJ 08933-7003



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22312-1450  
www.uspto.gov

JUN 21 2004

Mailed: June 21, 2004

#16

Audley A. Ciporcero, Jr.  
One Johnson & Johnson Plaza  
New Brunswick NJ 08933-7003

In Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,513,006

NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,513,006, which claims the human drug product TOPAMAX® (topiramate), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be five years.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Director will issue a certificate of extension, under seal, for a period of five years.

If the patent term extension were calculated using the Food and Drug Administration determination of the length of the regulatory review period published in the Federal Register of March 19, 2003 (68 Fed. Reg. 13315), the period of extension:

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (2984 - 0) + 860 \\ &= 2,352 \text{ days (6.4 years)}\end{aligned}$$

Since the regulatory review period began June 18, 1986, after the patent issued (April 23, 1985), the entire regulatory review period is considered in the above determination of the length of the extension period according to 35 U.S.C. § 156(c). No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The five year limitation of 35 U.S.C. § 156(g)(6)(A) applies in the present situation, however, because the patent was issued after the date of enactment of 35 U.S.C. § 156. Since the period of extension calculated under 35 U.S.C. § 156(c) for the patent cannot exceed five years under 35 U.S.C. § 156(g)(6)(A), the period of extension will be for five years.

The 14 year limitation of 35 U.S.C. § 156(c)(3) does not operate to further reduce the period of extension determined above.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.:	4,513,006
Granted:	April 23, 1985

UNITED STATES PATENT AND TRADEMARK OFFICE

(12) CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

(68) PATENT NO. : 4,513,006  
(45) ISSUED : April 23, 1985  
(75) INVENTOR : Bruce E. Maryanoff, et al.  
(73) PATENT OWNER : McNeil Lab, Inc.  
(95) PRODUCT : TOPAMAX® (topiramate)


This is to certify that an application under 35 U.S.C. § 156 has been filed in the United States Patent and Trademark Office, requesting extension of the term of U.S. Patent No. 4,513,006 based upon the regulatory review of the product TOPAMAX® (topiramate) by the Food and Drug Administration. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

(94) Five Years

from September 23, 2003, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the United States Patent and Trademark Office to be affixed this 23rd day of July 2004.

  
Jon W. Dudas  
Acting Under Secretary of Commerce for  
Intellectual Property and Acting Director of the  
United States Patent and Trademark Office



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re United States Patent 4,702,253

Patentee: Nappholz et al.

Attn: Box Patent Ext.

Issue Date: October 27, 1987

Assignee: Teletronics N.V.

**REQUEST FOR EXTENSION OF  
PATENT TERM UNDER 35 U.S.C. 156**

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

"Express Mail" mailing label number 80451430392  
Date of Deposit 12/10/91  
I hereby certify that this paper or fee is  
being deposited with the United States Postal  
Service "Express Mail First Office to Arrive" on  
service under 37 CFR 1.10 on the date indicated  
above and is addressed to the Commissioner of  
Patents and Trademarks, Washington, D.C. 20231.  
Diane Bivell  
(Typed or printed name of person mailing  
paper or fee)  
Diane Bivell  
(Signature of person mailing paper or fee)

Sir:

Pursuant to Section 201(a) of the Drug Price  
Competition and Patent Term Restoration Act of 1984, 35 U.S.C.  
156, Teletronics N.V. ("Teletronics") owner of the above-  
identified patent, hereby requests an extension of the patent  
term of U.S. Patent No. 4,702,253. The following information is  
submitted in accordance with 35 U.S.C. 156(d) and 37 CFR 1.740  
and follows the format set forth in Section 1.740.

(1) A complete identification of the approved product as by  
appropriate chemical and physical structure or characteristics:

The approved product is the META II, Model 1204 Cardiac  
Pacing System (hereinafter the "META II pacemaker"). The META II  
pacemaker is a system for maintaining and regulating the cardiac  
rate in patients exhibiting certain symptoms and indications for  
long term cardiac pacing. The META II pacemaker is responsive to  
certain physiological needs of the patient for increasing cardiac  
output. Specifically, the pacing rate of the META II pacemaker

is linearly related to minute ventilation.

A Summary of Safety and Effectiveness for the META II pacemaker is annexed as Appendix A. The related Physician's Manual is annexed as Appendix B. The items in Appendices A and B form a complete identification and description of the META II pacemaker system.

(2) A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred:

The regulatory review occurred under Section 515 of the Federal Food, Drug and Cosmetic Act ("FFDCA").

(3) An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred:

The META II pacemaker was approved by the Food And Drug Administration ("FDA") for commercial marketing pursuant to Section 515 of the FFDCA on October 11, 1991.

(4) In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it

was approved, and the provision of law under which it was approved:

Not applicable, the product is not a drug.

(5) A statement that the application is being submitted within the sixty-day period permitted for submission pursuant to § 1.720(f) and an identification of the date of the last day on which the application could be submitted:

The META II pacemaker was approved on October 11, 1991 and the last day within the sixty day period permitted for submission of an application for extension of a patent is December 10, 1991. As evidenced by the Certificate of Mailing by "Express Mail", this application is timely filed.

(6) A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue and the date of expiration:

Inventor: Tibor A. Nappholz, Mark Lubin,  
Harry L. Valenta, Jr.

U.S. Patent No. 4,702,253

Issued: October 27, 1987

Expiration Date: October 27, 2004

(7) A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings:

A copy of U.S. Patent No. 4,702,257 is attached herewith as Appendix C.

(8) A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or re-examination certificate issued in the patent:

A copy of the receipt of maintenance fee payment is annexed hereto as Appendix D.

(9) A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or a method of using or manufacturing the approved product:

Claims 1, 2, 3, 4, 5, 9, 10, 12, 13, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 and 28 read on the META II pacemaker, as follows:

The META II pacemaker is a metabolic demand pacer which senses minute volume and uses this parameter to control the standby rate. The electrode for pacing and minute volume measurement is situated in the main blood vessel and the right heart. The pacemaker case is on the chest wall. The measurement is done by injecting current from the ring to the case and measuring from the tip to the case. These two electrodes constitute 'first' and 'second' electrodes in claims 5, 10, 12, 14, 17, 23, 27 and 28. The position of the lead and measurement is as per claims 1, 13, 18, 21 and 22. The peaks of the ventilation are counted, averaged and summed as per claims 2 and

24. The long term average corresponds to the standby rate and the deviation to the increase from the standby rate is as per claims 3, 9, 16, 20, 25 and 26. The rate is only allowed to deviate to a preset maximum rate as per claims 4 and 19.

(10) A statement, beginning on a new page, of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

(v) For a patent claiming a medical device, the effective date of the investigational device exemption (IDE) and the IDE number, if applicable, or the date on which the applicant began the first clinical investigation involving the device if no IDE was submitted and an available substantiation of that date; the date on which the application for product approval or notice of completion of a product development protocol under section 515 of the Federal Food, Drug, and Cosmetic Act was initially submitted and the number of the application or protocol, and the date on which the application was approved or the protocol declared to be completed.

Telectronics did not obtain an IDE for the META II pacemaker nor did it undertake clinical studies for this device.

By letter dated July 19, 1990, and received at the FDA on or about July 20, 1990, Telectronic's licensee, Telectronics Pacing Systems, Inc., requested that its pre-market approval application ("PMA") which had been granted for a product identified as META MV Model 1202 Cardiac Pacing System, PMA 880038, be supplemented to enable introduction of the META II pacemaker. This application to supplement the existing PMA was

approved on October 11, 1991 under PMA 880038/513. Various correspondence with the FDA regarding this submission is submitted herewith as Appendices E - P.

(11) A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities:

During the applicable regulatory review period, Teletronics, through the activities of its licensee Teletronics Pacing Systems, Inc., was actively involved in obtaining pre-market approval for the META II pacemaker (Model 1204).

As discussed above, the supplement to the PMA to cover the META II pacemaker was submitted to the FDA by letter dated July 19, 1990 (Appendix E) and was received the next day. Representatives of Teletronics Pacing Systems, Inc. worked closely with the FDA in obtaining approval of the PMA Supplement. For example, on December 27, 1990, the FDA notified Teletronics Pacing Systems, Inc. that the PMA Supplement was approvable, subject to certain additional submissions. The December 27, 1990 letter (Appendix H) went on to set forth approximately 25 items, plus subparagraphs, which required action by Teletronics. On February 18, 1991 (Appendix J), Teletronics Pacing Systems, Inc. submitted its amendment to the PMA Supplement to respond to the deficiencies noted in the FDA Approval letter of December 27, 1990; a revised Summary of Safety and Effectiveness and a revised Physicians Manual for the Model 1204 were also submitted to the FDA. Additional amendments were submitted to the FDA on May 8,



June 25 and July 18, 1991.

In addition to responding to the FDA, Telectronics also modified the design of the Model 1204 for manufacturing purposes and changed the software.

Telectronics also arranged for the inspection of the manufacturing facilities for the META II pacemaker by FDA personnel.

(12) A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of the extension claimed, including how the length of extension was determined:

(a) Teletronics believes that the patent is eligible for extension under 35 U.S.C. 156(a) as follows:

Section 156(a) provides, in relevant part, that the term of a patent which claims a product shall be extended if (1) the term of the patent has not expired before an application for extension is submitted, (2) the term of the patent has never been extended, (3) an application for extension is submitted in accordance with 35 U.S.C. 156(d), (4) the product has been subject to a regulatory review period before its commercial marketing or use, (5) the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

In the present case, each of these elements is satisfied as indicated below:

(1) The term of U.S. Patent No. 4,702,253 expires on October 27, 2004. The present application has therefore been submitted before the expiration of the patent term.

(2) The term of this patent has never been extended.

(3) This application is submitted by Teletronics

N.V., the owner of record of the patent. This application is submitted in accordance with 35 U.S.C. 156(d), in that it is submitted within the sixty-day period beginning on October 11, 1991, the date that the product received permission for marketing from the FDA (see Appendix P). Further, the present application complies with the requirements of an application under 35 U.S.C. 156(d) and the applicable CFR sections, including 37 CFR § 1.740.

(4) As evidenced by the October 11, 1991 letter from the FDA (Appendix P), the product was approved in accordance with Section 515 of the Federal Food, Drug, and Cosmetic Act.

(5) Finally, and in accordance with 35 U.S.C. 156(a)(5)(A), Telectronics asserts that although the META MV Model 1202 Cardiac Pacemaker System was previously commercialized, the permission for the commercial marketing or use of the META II Model 1204 pacemaker (the product upon which the extension is sought) is the first permitted marketing or use of that product under the provision of law under which such regulatory review period occurred.

(b) Statement as to length of extension claimed.

The term of Patent No. 4,702,253 should be extended 349 days to October 11, 2005. This extension was determined on the following basis:

The calculation of a patent term extension for a medical device is set forth in 37 CFR § 1.777.

Rule 1.777(c) first requires that the length of the regulatory review period to be determined. This is the sum of the number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted (Rule 1.777(c)(1)), and the number of days in the period beginning on the date the application was initially submitted with respect to the device and ending on the date such application was approved (Rule 1.777(c)(2)). In the present case, there were no clinical investigations on humans involving the META II pacemaker, so that (c)(1) is inapplicable. Under (c)(2), there are 448 days between the date the application was originally submitted to the FDA for approval of the META II pacemaker (July 20, 1990) and the date when the PMA Supplement was approved (October 11, 1991). Thus, the length of the regulatory period is 448 days.

Rule 1.777(d) sets forth the term that the patent will be extended.

Under (d)(1), there may be certain subtractions from the regulatory review period determined pursuant to paragraph

(c)(1) and (c)(2). In the present case, no subtractions are applicable since the number of days in the periods of paragraphs (c)(1) and (c)(2) were not on or before the date on which the patent issued ((d)(1)(i)), since applicant acted with due diligence ((d)(1)(ii)), and since no half day reduction is warranted under (d)(1)(iii), there being no days under (c)(1).

Next, Rule 1.777(d)(2) - (4) requires that certain dates be calculated and compared. Under (d)(2) adding 448 days to October 27, 2004, the original term of the patent (there being no terminal disclaimer), provides a date of January 18, 2006. Under (d)(3), adding 14 years to the date of approval of the application under Section 515 of the Act (14 years from October 11, 1991), provides a date of October 11, 2005. Comparing the periods obtained pursuant to (d)(2) and (d)(3) to obtain the earlier date provides a date of October 11, 2005. Under (d)(5), since the original patent issued after September 24, 1984, five years must be added to the original expiration date of the patent (October 27, 2004) and compared to the date obtained pursuant to paragraph (d)(4). Adding five years to the expiration date of the patent presents a date of October 27, 2009. This date is later than the date of paragraph (d)(4), which is October 11, 2005.

Accordingly, the patent should be extended 349 days to October 11, 2005, this being the number of days between the normal expiration of the patent, October 27, 2004, and the

earliest date determined under (d)(4), that is, 14 years from the date the supplement to the PMA was approved, October 11, 1991.

(13) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and to the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to any determination of entitlement to the extension sought (see § 1.765).

Teletronics is unaware of any such information other than that already presented in this application, including the attached exhibits.

Applicant is submitting the prescribed fee for receiving and acting upon the application in the amount of \$600. The Office is authorized to charge any underpayment or to credit any overpayment to our Deposit Account No. 07-1730.

The office is requested to direct all inquiries and correspondence relating to this application for patent term extension to Barry A. Cooper, Esq. and/or Michael I. Rackman, Esq. c/o Gottlieb, Rackman & Reisman, P.C., 1430 Broadway, New York, New York 10018, (212) 869-2890.

Teletronics is submitting a duplicate copy of this application, certified as such.

The undersigned declares as follows:

(a) He is a registered patent attorney authorized to practice before the Patent and Trademark Office and has general authority from Teletronics N.V., the owner of record of U.S. Patent No. 4,702,253, to act in its behalf in patent matters;

(b) He has reviewed and understands the contents of

the application being submitted concurrently herewith, namely, an application for extension of patent term for U.S. Patent No. 4,702,253;

(c) He believes that the patent is subject to the extension sought pursuant to 37 CFR § 1.710;

(d) He believes an extension of the length claimed is justified under 35 USC 156 and the applicable regulations;

(e) He believes the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 35 CFR § 1.720; and

(f) He declares that all statements made herein of his own knowledge are true and that all statements made upon information and belief are believed to be true and that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, Section 1001 of the United States Code, and that such willful false statements may jeopardize this application.

GOTTLIEB, RACKMAN & REISMAN, P.C.  
Attorneys for Telectronics N.V.  
1430 Broadway  
New York, New York 10018  
(212) 869-2890

By: 

Barry A. Cooper  
Reg. No. 25,204

Dated: New York, New York  
December 10, 1991



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re United States Patent 4,702,253

Patentee: Nappholz et al.

Attn: Box Patent Ext.

Issue Date: October 27, 1987

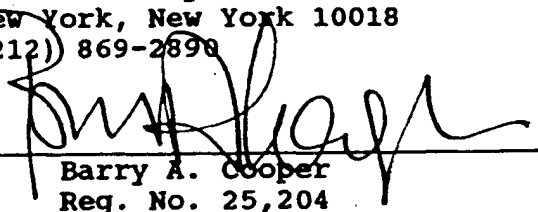
Assignee: Telectronics N.V.

**CERTIFICATION**

The undersigned hereby certifies that the attached document is a duplicate of the Request For Extension Of Patent Term Under 35 U.S.C. 156 of U.S. Patent No. 4,702,253, filed concurrently herewith.

GOTTLIEB, RACKMAN & REISMAN  
Attorneys for Telectronics N.V.  
1430 Broadway  
New York, New York 10018  
(212) 869-2890

By: \_\_\_\_\_

  
Barry A. Cooper  
Reg. No. 25,204

Dated: New York, New York  
December 10, 1991



**UNITED STATES DEPARTMENT OF COMMERCE**  
**Patent and Trademark Office**  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

DEC 16 1991

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

Dear Mr. Wilson:

The enclosed application for patent term extension of U.S. Patent No. 4,702,253 issued on October 27, 1987, was filed on December 10, 1991, under 35 USC § 156.

Your assistance is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC § 156 (g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 USC § 156 (d) (2) (A).

Our review of the application to date indicates that the subject matter would be eligible for extension of the patent term under 35 USC § 156.

*C.E. Van Horn*

Charles E. Van Horn  
Patent Policy & Programs Administrator  
Office of the Assistant Commissioner for Patents

cc: Barry A. Cooper  
Gottlieb, Rackman & Reisman, P.C.  
1430 Broadway  
New York, NY 10018



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

RECEIVED

92 MAR 20 PM 1:43

Food and Drug Administration  
Rockville MD 20857

MAR 18 1992

DEPUTY ASSISTANT  
COMMISSIONER FOR PATENT

Re: META II, Model 1204,  
Cardiac Pacing System  
Docket No. 92E-0004

Charles E. Van Horn  
Patent Policy and Projects Administrator  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

Dear Mr. Van Horn:

This is in regard to the application for patent term extension for U.S. Patent No. 4,702,253 filed by Telectronics N.V. , under 35 U.S.C. 156. The medical device claimed by the patent is the META II, Model 1204, Cardiac Pacing System, Premarket Application (PMA) number P880038/S13.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of this product under section 515(d) of the Federal Food, Drug, and Cosmetic Act.

The PMA was approved on October 11, 1991, which makes the submission of the patent term extension application on December 10, 1991, timely within the meaning of 35 U.S.C. 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Barry A. Cooper, Esq.



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

FEB 10 1993

Barry A. Cooper  
Gottlieb, Rackman & Reisman, P.C.  
1430 Broadway  
New York, NY 10018

Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,702,253

### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,702,253 issued October 27, 1987, which claims the medical device Meta II, is eligible for patent term extension under 35 USC § 156. The period of extension has been determined to be 349 days.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of January 27, 1993. The January 27, 1993, notice corrected an original notice of the regulatory review period published in the Federal Register of May 13, 1992. Under 35 USC § 156 (c):

$$\begin{aligned}\text{Period of Extension} &= 1/2 (\text{Testing Phase}) + \text{Approval Phase} \\ &= 1/2 (0) + 449 \\ &= 449 \text{ days}\end{aligned}$$

Since the regulatory review period began after the patent issue date, the entire period has been considered. No determination of a lack of due diligence was made.

The 14 year exception of 35 USC § 156 (c) (3) operates to limit the term of extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the approved product (October 11, 1991) when added to the period of extension calculated above (449 days) cannot exceed fourteen years. The period of extension is thus limited to October 11, 2005, by operation of 35 USC § 156 (c) (3). Since the patent term of seventeen years (35 USC § 154) would expire on October 27, 2004, the period of extension is the number of days to extend the term of the patent from its expiration date to and including October 11, 2005, or 349 days.

The limitations of 35 USC § 156 (g) (6) do not operate to further reduce the period of extension determined above.

U.S. Patent No. 4,702,253

A single request for reconsideration of this final determination as to eligibility and the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136 (a) are not applicable to this time period. In the absence of such request for reconsideration, the Commissioner will issue to the applicant for extension of the term of Patent No. 4,702,253 a certificate of extension, under seal, for a period of 349 days.

Upon issuance of the certificate of extension the following information will be published in the Official Gazette:

U.S. Patent No.:	4,702,253
Granted:	October 27, 1987
Applicant:	Tibor A. Nappholz et al
Owner of Record:	Teletronics N.V.
Title:	METABOLIC-DEMAND PACEMAKER AND METHOD OF USING THE SAME TO DETERMINE MINUTE VOLUME
Classification:	128/419PG
Product Trade Name:	Meta II
Term Extended:	349 days

*C.E. Van Horn*

Charles E. Van Horn  
Patent Policy & Projects Administrator  
Office of the Assistant Commissioner for Patents

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 11-44  
Rockville, MD 20857

RE: Meta II

FDA Docket No.: 92E - 0004

**UNITED STATES PATENT AND TRADEMARK OFFICE**

**CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156**

**PATENT NO.:** 4,702,253  
**DATED:** October 27, 1987  
**INVENTORS:** Tibor A. Nappholz et al.  
**PATENT OWNER:** Teletronics N.V.

This is to certify that there has been presented to the

**COMMISSIONER OF PATENTS AND TRADEMARKS**

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

**349 DAYS**

with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 20th day of May 1993.

Michael K. Kirk  
Acting Commissioner of Patents and Trademarks



17  
U.S. PATENT No. 4,830,010  
ATTORNEY DOCKET NO. 040131-0003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 4,830,010  
Issued: May 16, 1989

Inventor: Barry J. MARSHALL

BOX: PATENT TERM EXTENSION

Serial No.: 07/147,058  
Filed: January 22, 1988

For: METHODS FOR THE DIAGNOSIS OF GASTROINTESTINAL DISORDERS

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

**APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. § 156**

Applicant, Meretekdiagnostics, inc., a corporation organized and existing under the laws of the State of Delaware, represents that it has been appointed a Special Power of Attorney, a copy of which is attached hereto as Exhibit 1, from Dr. Barry J. Marshall, the owner of record of the above-identified patent, to prepare, file, and prosecute an Application for Patent Term Extension in the United States Patent and Trademark Office in respect of United States Letters Patent No. 4,830,010, granted to Dr. Barry J. Marshall on May 16, 1989, for METHODS FOR THE DIAGNOSIS OF GASTROINTESTINAL DISORDERS.

Applicant, acting through its duly authorized attorney, whose power to act on behalf of Applicant is filed simultaneously herewith as Exhibit 2, hereby submits this Application for Extension of Patent Term under 35 U.S.C. § 156 by providing the following information pursuant to 37 C.F.R. § 1.740. For convenience, the information contained in this Application will be presented according to the format set forth in 37 C.F.R. § 1.740(a).

(1) This Application for Patent Term Extension is based upon the regulatory review period before the Food and Drug Administration ("FDA") of Applicant's approved product,  $^{13}\text{C}$ -labeled urea. The only active ingredient in the approved product is  $^{13}\text{C}$ -urea.

$^{13}\text{C}$  is a natural, stable, nonradioactive carbon isotope that constitutes 1.1% of all carbon in nature. It can not be created nor destroyed. Unlike radioactive  $^{14}\text{C}$ ,  $^{13}\text{C}$  is a stable isotope and does not emit radiation.

$^{13}\text{C}$ -labeled urea is designated chemically as  $^{13}\text{CO}(\text{NH}_2)_2$  and has a molecular weight of 102.07. Urea is the diamide of carbonic acid, and is also known as carbamide, carbamimidic acid, carbonyl diamide, carbonyldiamine, and isourea.

Urea may be obtained artificially by heating a solution of ammonium cyanate. In addition, liquid ammonia and liquid carbon dioxide at 1750-3000 psi and 160-200°C react to form ammonium carbamate,  $\text{NH}_4\text{CO}_2\text{NH}_2$ , which decomposes at lower pressure (about 80 psi) to urea and water.

(2) The approved product,  $^{13}\text{C}$ -labeled urea, was subject to regulatory review under Federal Food, Drug, and Cosmetic Act ("F.F.D.C.A.") Section 505 (21 U.S.C. § 355).

(3)  $^{13}\text{C}$ -labeled urea received permission for commercial use under the F.F.D.C.A. on September 17, 1996. See Exhibit 3, which is a copy of the FDA approval letter.

(4)  $^{13}\text{C}$ -labeled urea has not been previously approved for commercial marketing or use under the F.F.D.C.A., the Public Health Service Act, or the Virus-Serum-Toxin Act.



(5) This Application for Patent Term Extension is being filed within the sixty day period permitted for submission pursuant to 37 C.F.R. § 1.720(f). The Applicant received approval of its New Drug Application ("NDA") # 20-586 for the approved product, <sup>13</sup>C-labeled urea, from the Center for Drug Evaluation and Research ("CDER") in a letter dated September 17, 1996. See Exhibit 3. The last day of the sixty day period following approval during which this Application for Patent Term Extension may be filed is November 16, 1996. Because this day falls on a Saturday, the last day for filing an Application for Patent Term Extension is Monday, November 18, 1996.

(6) The complete identification of the patent for which extension is being sought is as follows:

Inventor:	Barry J. Marshall
Patent No.	4,830,010
Filing Date:	January 22, 1988
Issue Date:	May 16, 1989
Expiration Date:	May 16, 2006

(7) A complete copy of the patent identified in paragraph (6) above is attached hereto as Exhibit 4.

(8) No Disclaimer, Certificate of Correction, or Reexamination Certificate has been issued with regard to U.S. Patent No. 4,830,010. Two maintenance fee payments have been paid for U.S. Patent No. 4,830,010. Attached hereto as Exhibit 5 is a computer print out of public records showing that the first and second maintenance fee payments were paid on September 24, 1992, and September 24, 1996, respectively.

(9) U.S. Patent No. 4,830,010 claims the use of the approved product,  $^{13}\text{C}$ -labeled urea, in a method for the diagnosis of a gastrointestinal disorder of the upper gastrointestinal tract caused or mediated by bacteria. In the claimed methods, an amount of isotope-labeled urea is administered to a subject, followed by analyzing the breath of the subject for isotope-labeled carbon dioxide, isotope-labeled ammonia, or both hydrolysis products of urea, in which the presence of such hydrolysis products is a positive indication of a gastrointestinal disorder.

In the presence of urease due to gastric bacterial infection, such as *Helicobacter pylori* ("*H. pylori*") (formerly known as *Campylobacter pyloridis*, which is the name used in the patent claims), ingested  $^{13}\text{C}$ -labeled urea is decomposed to  $^{13}\text{CO}_2$  and  $\text{NH}_4^+$ . The  $^{13}\text{CO}_2$  is absorbed in the blood and then exhaled in the breath. This results in an increase in the ratio of  $^{13}\text{CO}_2/^{12}\text{CO}_2$  in a test breath sample, which is considered a positive diagnostic indication of a gastrointestinal disorder caused by a gastric bacterial infection.

The following is a chart showing the applicable claim number and corresponding claim language which reads on a method of using the approved product,  $^{13}\text{C}$ -labeled urea.

Claim No.	Claim Language
1	A method for the diagnosis in a human or lower animal subject of a gastrointestinal disorder of the upper gastrointestinal tract caused or mediated by the bacteria <i>Campylobacter pyloridis</i> , said method comprising the steps of administering to said subject a safe and effective amount of isotope-labeled urea, and analyzing the breath of said subject for the presence of isotope-labeled carbon dioxide, isotope-labeled ammonia, or both hydrolysis products, wherein the presence of either or both said hydrolysis products is a positive indication of said gastrointestinal disorder in said subject.

2	A method for the diagnosis in a human or lower animal subject of a gastrointestinal disorder of the upper gastrointestinal tract caused or mediated by bacteria which result in the gastric materials of the human or lower animal to contain relatively large quantities of urease, said method comprising the steps of administering to said subject a safe and effective amount of isotope-labeled urea, and analyzing the breath of said subject for the presence of isotope-labeled carbon dioxide, isotope-labeled ammonia, or both hydrolysis products, wherein the presence of either or both said hydrolysis products is a positive indication of said gastrointestinal disorder in said subject.
3	A method for the diagnosis of a gastrointestinal disorder of the upper gastrointestinal tract caused or mediated by bacteria resulting in the gastric materials containing relatively large quantities of urease in a human or lower animal subject, according to claim 2 wherein said analyzing step involves analyzing the breath of said subject for the presence of isotope-labeled carbon dioxide hydrolysis product of said isotope-labeled urea.
5	A method for the diagnosis of a gastrointestinal disorder of the upper gastrointestinal tract caused or mediated by bacteria resulting in the gastric materials containing relatively large quantities of urease in a human or lower animal subject, according to claim 3, wherein said urea is isotope-labeled with carbon-13 isotope.

All of claims 1, 2, 3, and 5 of U.S. Patent No. 4,830,010 read on using the approved product,  $^{13}\text{C}$ -labeled urea, in the claimed process. For example, claims 1 and 2 recite the use of "isotope-labeled urea," which reads on the use of  $^{13}\text{C}$ -labeled urea, and analyzing the breath of the patient for the presence of "isotope-labeled carbon dioxide," which when the isotope-labeled urea is  $^{13}\text{C}$ -urea will be  $^{13}\text{CO}_2$ . Claim 3 recites the method of claim 2 in which the breath of the patient is analyzed for the presence of "isotope-labeled carbon dioxide," which when the isotope-labeled urea of claim 2 is  $^{13}\text{C}$ -urea will be  $^{13}\text{CO}_2$ ; and claim 5 recites the method of claim 3 in which the urea is "isotope-labeled with carbon-13 isotope," which reads on  $^{13}\text{C}$ -labeled urea. Accordingly, all of claims 1, 2, 3, and 5 of U.S. Patent No. 4,830,010 read on using the FDA-approved product,  $^{13}\text{C}$ -labeled urea, in the claimed process for detecting gastrointestinal disorders.

(10) The relevant dates and information pursuant to 35 U.S.C. § 156(g) necessary to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

- (a) U.S. Patent No. 4,830,010 was issued on May 16, 1989, and claims a method of using the approved product,  $^{13}\text{C}$ -labeled urea;
- (b) Investigational New Drug Application ("IND") # 26861 was filed with the FDA by *Meretekdiagnostics, inc.*'s collaborator, Abbott Laboratories, as detailed below in paragraph (11), on December 20, 1989, and became effective on January 19, 1990. *Meretekdiagnostics, inc.* began testing in collaboration with Abbott Laboratories under Abbott's IND # 26861 on October 21, 1993;
- (c) New Drug Application ("NDA") for  $^{13}\text{C}$ -labeled urea was submitted on May 11, 1995, and assigned NDA # 20-586; and
- (d) NDA # 20-586 for  $^{13}\text{C}$ -labeled urea was approved by the FDA on September 17, 1996.

(11) A brief description of the significant activities undertaken by the marketing applicant, *Meretekdiagnostics, inc.*, and its collaborator, Abbott Laboratories ("Abbott"), a corporation of the State of Illinois and having a principle place of business at 100 Abbott Park Road, Abbott Park, Illinois 60064-3500, is attached hereto as Exhibit 6. Exhibit 6 is a chronology of events and major communications with the FDA from October 21, 1993, the date *Meretekdiagnostics, inc.* began testing in collaboration with Abbott under Abbott's IND # 26861, to September 17, 1996, the date the FDA approved NDA # 20-586.

(12) Applicant is of the opinion that U.S. Patent No. 4,830,010 is eligible for extension under 35 U.S.C. § 156 because it satisfies all the requirements for such extension as follows:

- (a) 35 U.S.C. § 156(a)  
U.S. Patent No. 4,830,010 claims a method of using a drug product.
- (b) 35 U.S.C. § 156(a)(1)  
The term of U.S. Patent No. 4,830,010 has not expired before submission of this Application.
- (c) 35 U.S.C. § 156(a)(2)

The term of U.S. Patent No. 4,830,010 has never been extended.

- (d) 35 U.S.C. § 156(a)(3)  
The Application for Patent Term Extension is submitted by the authorized agent of the owner of record in accordance with the requirements of 35 U.S.C. § 156(d) and 37 C.F.R. § 1.710 *et seq.*
- (e) 35 U.S.C. § 156(a)(4)  
The approved product, <sup>13</sup>C-labeled urea, has been subject to a regulatory review period before its commercial marketing or use.
- (f) 35 U.S.C. § 156(a)(5)(A)  
The commercial marketing or use of the approved product, <sup>13</sup>C-labeled urea, after the regulatory review period, is the first permitted commercial marketing or use of the approved product under the provisions of the F.F.D.C.A. (21 U.S.C. § 355), under which such regulatory review period occurred.
- (g) 35 U.S.C. § 156(c)(4)  
No other patent has been extended for the same regulatory review period for the approved product, <sup>13</sup>C-labeled urea.

(12-A) The length of the extension of the patent term of U.S. Patent No. 4,830,010 claimed by Applicant is 780 days, which extends the term of U.S. Patent No. 4,830,010 from the expiration date of May 16, 2006, to July 4, 2008. The length of the extension was determined pursuant to 37 C.F.R. § 1.775 as follows:

- (a) The regulatory review period under 35 U.S.C. § 156(g)(1)(B) began on October 21, 1993, the day Applicant Meretekdiagnostics, inc. began testing the approved product, <sup>13</sup>C-urea, in collaboration with Abbott under Abbott's IND # 26861. Accordingly, Applicant claims benefit of activities conducted by Applicant under IND # 26861 as of October 21, 1993. Applicant does not claim benefit of the time period from the effective date of January 19, 1990, of IND # 26861 up until October 21, 1993. The regulatory review period ended on September 17, 1996, which is the date NDA # 20-586 was approved by the FDA, for a total number of 1063 days, which is the sum of (i) and (ii) below:

- (i) The period of review under 35 U.S.C. § 156(g)(1)(b)(i), the "testing period," began on October 21, 1993, the day Applicant *Meretekdiagnostics, inc.* began testing the approved product, <sup>13</sup>C-urea, in collaboration with Abbott under Abbott's IND # 26861, and ended on May 11, 1995, which is the date NDA # 20-586 was filed with the FDA, which is 567 days, and
- (ii) The period of review under 35 U.S.C. § 156(g)(1)(B)(ii), the "application period," began on May 11, 1995, which is the date NDA # 20-586 was filed with the FDA, and ended on September 17, 1996, which is the date NDA # 20-586 was approved by the FDA, which is 496 days;
- (b) The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in subparagraph (12-A)(a) above, or 1063 days, less 283 days, which is the sum of:
  - (i) The number of days in the regulatory period which were on or before the date on which the patent issued, May 16, 1989, which is zero (0) days;
  - (ii) The number of days in which Applicant did not act with due diligence, which is zero (0) days;
  - (iii) One-half the number of days determined in subparagraph (12-A)(a)(i) after the patent issued or 283 days;

for a total extension period of 780 days.
- (c) The number of days in the total extension period as determined in subparagraph (12-A)(b), or 780 days, when added to the original term of the patent would result in an expiration date of July 4, 2008 (May 16, 2006 + 780 days = July 4, 2008).
- (d) Fourteen years when added to the date of NDA approval (September 17, 1996), results in the date of September 17, 2010.
- (e) The earlier date as determined in subparagraphs (12-A)(c) and (12-A)(d) is July 4, 2008.

ATTORNEY DOCKET NO. 040131-0003

U.S. Patent No. 4,830,010

Page 9

- (f) Therefore, the length of extension of patent term claimed by Applicant is 780 days. The date of termination of the extended patent term is not more than 14 years from the date of NDA approval.

(13) The Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determinations to be made relative to the Application for Patent Term Extension.

(14) A check in the amount of \$ 1,090.00, representing the full payment of the application fee as set forth in 37 C.F.R. § 1.20(j), is enclosed. The Commissioner is hereby authorized to charge any deficiency in the payment of the required fee or credit any overpayment to Deposit Account 13-4520.

- (15) All inquiries and correspondence should be directed to:

Michele M. Schafer, Esq.  
Morgan, Lewis & Bockius LLP  
1800 M Street, N.W.  
Washington, D.C. 20036

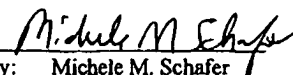
Telephone calls should be directed to Michele M. Schafer at 202-467-7614.

- (16) A duplicate of the application papers, certified as such, is attached hereto.

(17) Submitted herewith is a Declaration pursuant to 37 C.F.R. § 1.740(b), attached hereto as Exhibit 7.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS

  
By: Michele M. Schafer  
Reg. No. 34,717

Dated: November 18, 1996

ATTORNEY DOCKET NO. 040131-0003

U.S. Patent No. 4,830,010

Page 10


**CERTIFICATION**

The undersigned hereby certifies that this Application for Extension of Patent Term

Under 35 U.S.C. § 156, including its Exhibits and supporting papers, is being submitted as one original along with a duplicate copy thereof.

Respectfully submitted,

**MORGAN, LEWIS & BOCKIUS**

  
By: Michele M. Schafer  
Reg. No. 34,717

Dated: November 18, 1996



U.S. PATENT No. 4,830,010  
ATTORNEY DOCKET NO. 040131-0003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 4,830,010  
Issued: May 16, 1989

Inventor: Barry J. MARSHALL

Serial No.: 07/147,058  
Filed: January 22, 1988

For: METHODS FOR THE DIAGNOSIS OF GASTROINTESTINAL DISORDERS

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

**DECLARATION UNDER 37 C.F.R. § 1.740(b)**

The undersigned attorney for Meretekdiagnostics, inc., who is the Applicant for the Application for Extension of Patent Term Under 35 U.S.C. § 156 with regard to U.S. Patent No. 4,830,010, hereby declares as follows:

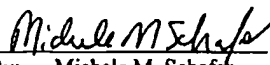
- (1) That I am a patent attorney authorized to practice before the United States Patent and Trademark Office and that my registration number is 34,717;
- (2) That I make this declaration as an attorney acting on behalf of and with authority of Meretekdiagnostics, inc., a corporation organized and existing under the laws of the State of Delaware, and having a principle place of business at Medical Towers Building, 1709 Dryden Road, Suite 1513, Houston, Texas 77030, which is the exclusive licensee of U.S. Patent No. 4,830,010, such authority being filed herewith;

- (3) That Meretekdiagnostics, inc. has been appointed a Special Power of Agent from Barry J. Marshall, the owner of record of U.S. Patent No. 4,830,010, to prepare, file, and prosecute an Application for Patent Term Extension in the United States Patent and Trademark Office in respect of U.S. Patent No. 4,830,010;
- (4) That I have reviewed and understand the contents of the Application submitted herewith pursuant to 35 U.S.C. § 156 and 37 C.F.R. § 1.740;
- (5) That, based on information and belief, I believe an extension of the length claimed is fully justified under 35 U.S.C. § 156; and
- (6) That I believe that the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 35 U.S.C. § 156 and 37 C.F.R. § 1.720.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of U.S. Patent No. 4,830,010 or any extension of patent term issuing thereon.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS

  
By: Michele M. Schafer  
Reg. No. 34,717

Dated November 18, 1996



107 DOL III Pat. Term Exten. 11/7

U.S. PATENT No. 4,830,010  
ATTORNEY DOCKET NO. 040131-0003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.: 4,830,010  
Issued: May 16, 1989

Inventor: Barry J. MARSHALL

BOX: PATENT TERM EXTENSION

Serial No.: 07/147,058  
Filed: January 22, 1988

For: METHODS FOR THE DIAGNOSIS OF GASTROINTESTINAL DISORDERS

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

RECEIVED  
NOV 27 1996  
OFFICE OF COMMISSIONER  
OF PATENTS

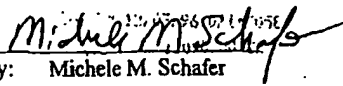
**TRANSMITTAL OF APPLICATION FOR EXTENSION  
OF PATENT TERM UNDER 35 U.S.C. § 156**

Transmitted herewith is an Application for Extension of Patent Term under 35 U.S.C.  
§ 156 with regard to U.S. Patent No. 4,830,010, including Exhibits 1-7.

The U.S. Patent and Trademark Office is authorized to charge Deposit Account No. 13-4520 pursuant to 37 C.F.R. § 1.20(n) for any fees not covered by the enclosed check in the amount of \$ 1,090.00. The Commissioner is hereby authorized to charge any additional fees which may be required or credit any overpayment to Deposit Account No. 13-4520. A duplicate copy of this authorization is attached.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS

  
By: Michele M. Schafer  
Reg. No. 34,717

Dated: November 18, 1996

DEC 12 1996



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HPY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 15-22  
Rockville, MD 20857

#19

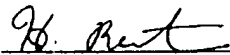
Dear Mr. Wilson:

The attached application for patent term extension of U.S. Patent No. 4,830,010, was filed on November 18, 1996, under 35 U.S.C. § 156. U.S. Patent No. 4,830,010 issued on May 16, 1989 from an application that claimed priority to an application that was filed on April 4, 1986. Accordingly, the original expiration date of the patent is May 16, 2006.

The assistance of your Office is requested in confirming that the product identified in the application, <sup>13</sup>C-labeled urea, has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156.

Inquiries regarding this communication should be directed to Karin Tyson at (703) 306-3159.

  
Hiram H. Bernstein  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Project

cc: Michele M. Schefer, Esq.  
Morgan, Lewis & Bockius LLP  
1800 M Street, N.W.  
Washington, D.C. 20036

kt



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

RECEIVED

#20

FEB 21 1997

FEB 24 1997

Re: Meretek Breath Test  
Docket No. 96E-0505

Stephen G. Kunin  
Deputy Assistant Commissioner for  
Patent Policy and Projects  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

PATENT EXTENSION  
A/C PATENTS

Dear Mr. Kunin:

This is in regard to the application for patent term extension for U.S. Patent No. 4,830,010 filed by Meretekdiagnostics, Inc. under 35 U.S.C. § 156. The human drug product claimed by the patent is Meretek Breath Test (urea, c-13), which was assigned New Drug Application (NDA) No. 20-586.

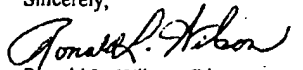
A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in Glaxo Operations UK Ltd. v. Quigg, 706 F. Supp 1224 (E.D. Va. 1989), aff'd, 894 F. 2d 392 (Fed. Cir. 1990).

The NDA was approved on September 17, 1996, which makes the submission of the patent term extension application on November 18, 1996, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

  
Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Michele M. Schafer, Esq.  
Morgan, Lewis, & Bockius, L.L.P.  
1800 M. Street, NW  
Washington, DC 20036



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

JAN 26 1998

Michele M. Schafer, Esq.  
Morgan, Lewis & Bockius LLP  
1800 M Street, N.W.  
Washington, D.C. 20036

In Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,830,010

#25

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,830,010, which claims the method of use of the human drug product MERETEK UBT™ Breath Test (<sup>13</sup>C-labeled Urea), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 1,260 days. U.S. Patent No. 4,830,010 has an original expiration date of May 16, 2006, subject to the provisions of 35 U.S.C. § 41(b). Accordingly, extension of the patent for 1,260 days will result in an extended expiration date of October 27, 2009.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of April 4, 1997 (62 Fed. Reg. 16,166). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (1,527) + 496 \\ &= 1,260 \text{ days (3.45 years)}\end{aligned}$$

Since the regulatory review period began March 7, 1991, after the patent issue date (May 16, 1989), the entire period has been considered in the above determination. No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

Neither the five year limitation of 35 U.S.C. § 156(g)(6)(A) nor the 14 year limitation of 35 U.S.C. § 156(c)(3) operate to reduce the period of extension determined above.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Commissioner will issue a certificate of extension, under seal, for a period of 1,259 days.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.	:	4,830,010
Granted	:	May 16, 1989
Original Expiration Date	:	May 16, 2006

U.S. Patent No. 4,830,010

Page 2

Applicant	:	Barry J. Marshall
Owner of Record	:	Barry J. Marshall
Title	:	Methods for the Diagnosis of Gastrointestinal Disorders
Classification	:	128/630
Product Trade Name	:	Meretek UBT™ Breath Test ( <sup>13</sup> C- labeled Urea)
Term Extended	:	1,260 days
Expiration Date of Extension	:	October 27, 2009

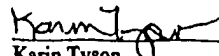
Any correspondence with respect to this matter should be addressed as follows:

By mail: Assistant Commissioner for Patents  
Box Patent Ext.  
Washington, D.C. 20231

By FAX: (703) 308-6916  
Attn: Special Program Law Office

By hand: One Crystal Park, Suite 520  
2011 Crystal Drive  
Arlington, VA

Telephone inquiries related to this determination should be directed to the undersigned at (703) 306-3159.



Karin Tyson  
Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 15-22  
Rockville, MD 20857

RE: Meretek UBT™ Breath Test  
(<sup>13</sup>C-labeled Urea)  
FDA Docket No.: 96E-0505

**UNITED STATES PATENT AND TRADEMARK OFFICE**

**CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156**

**PATENT NO.:** 4,702,253  
**DATED:** October 27, 1987  
**INVENTORS:** Tibor A. Nappholz et al.  
**PATENT OWNER:** Teletronics N.V.

This is to certify that there has been presented to the

**COMMISSIONER OF PATENTS AND TRADEMARKS**

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

**349 DAYS**

with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 20th day of May 1993.

A handwritten signature in cursive script, reading "Michael K. Kirk".

**Michael K. Kirk**  
Acting Commissioner of Patents and Trademarks



Docket No.: 149-026EX

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 4,836,217 : Attention: BOX PATENT EXT  
Issued: June 6, 1989 :  
Inventor: Torkel I. Fischer :  
Assignee: Pharmacia AB :  
For: HYPERSENSITIVITY TEST MEANS :

RECEIVED  
JAN 25 1995  
SPECIAL PROGRAMS OFFICE  
DAC FOR PATENTS

APPLICATION FOR EXTENSION OF PATENT TERM  
UNDER 35 USC 156

Honorable Commissioner of  
Patents and Trademarks  
Washington, D. C. 20231

Sir:

Applicant Pharmacia AB hereby applies for extension of the term of the Fischer U.S. Patent No. 4,836,217. Dr. Torkel Fischer is the owner of U.S. Patent No. 4,836,217. Pharmacia AB is the exclusive licensee of the patent and, by virtue of the Appointment of Agent executed by Dr. Fischer and submitted herewith in Appendix A, is Dr. Fischer's agent to apply for an extension of the patent term of U.S. Patent No. 4,836,217 under 35 USC 156 in the U.S. Patent and Trademark Office.

This application is submitted in accordance with the requirements of 35 USC 156 and 37 CFR 1.740.

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U.S. Patent No. 4,836,217

**I. IDENTIFICATION OF APPROVED PRODUCT**

The approved product is an Allergen Patch Test containing two allergen patch test panels. Each panel contains 12 allergen or allergen mix patches. To form the Allergen Patch Test, each allergen or allergen mix is uniformly dispersed in a film-forming polymer which is coated onto a polyester sheet. A patch is cut from the sheet and 24 patches, each containing a specific allergen or allergen mix dispersed in a dry film of the film-forming polymer, are assembled onto two strips or panels of surgical tape as follows:

PANEL 1		
PATCH NO.	ALLERGEN OR ALLERGEN MIX	FILM-FORMING POLYMER
1	Nickel sulfate, hexahydrate, equivalent to 0.036 mg nickel/patch	hydroxypropyl cellulose
2	Wool alcohols, equivalent to 0.81 mg wool alcohols/patch	polyvidone
3	Neomycin sulfate, equivalent to 0.19 mg neomycin sulfate/patch	methylcellulose
4	Potassium dichromate, equivalent to 0.0067 mg chromium/patch	hydroxypropyl cellulose
5	Caine Mx, equivalent to 0.49 mg caine mix/patch	polyvidone
6	Fragrance Mix, equivalent to 0.35 mg fragrance mix/patch	hydroxypropyl cellulose and B-cyclodextrin
7	Colophony, equivalent to 0.69 mg colophony/patch	hydroxypropyl cellulose

U.S. Patent No. 4,836,217

PANEL 1		
PATCH NO.	ALLERGEN OR ALLERGEN MIX	FILM-FORMING POLYMER
8	Epoxy resin, equivalent to 0.032 mg diglycidylether of bisphenol-A/patch	hydroxypropyl cellulose
9	Quinoline mix, equivalent to 0.154 mg quinoline mix/patch	hydroxypropyl cellulose
10	Balsam of Peru, equivalent to 0.65 mg Balsam of Peru/patch	polyvidone
11	Ethylenediamine dihydrochloride, equivalent to 0.018 mg ethylenediamine/patch	methylcellulose
12	Cobalt dichloride, equivalent to 0.0040 mg cobalt/patch	hydroxypropyl cellulose

PANEL 2		
PATCH NO.	ALLERGEN OR ALLERGEN MIX	FILM-FORMING POLYMER
13	p-tert Butylphenol formaldehyde resin, equivalent to 0.032 mg p-tert butylphenol formaldehyde/patch	hydroxypropyl cellulose
14	Paraben Mix, equivalent to 0.81 mg paraben mix/patch	polyvidone
15	Carba Mix, equivalent to 0.20 carba mix/patch	hydroxypropyl cellulose
16	Black Rubber Mix, equivalent to 0.081 mg black rubber mix/patch	polyvidone
17	Cl+Me-Isothiazolinone, equivalent to 0.0032 mg Cl+Me-Isothiazolinone/patch	polyvidone

U.S. Patent No. 4,836,217

PANEL 2		
PATCH NO.	ALLERGEN OR ALLERGEN MIX	FILM-FORMING POLYMER
18	Quaternium-15, equivalent to 0.081 mg quaternium-15/patch	hydroxypropyl cellulose
19	Mercaptobenzothiazole, equivalent to 0.061 mg mercaptobenzothiazole/patch	polyvidone
20	p-Phenylenediamine, equivalent to 0.073 mg p-phenylenediamine/patch	polyvidone
21	Formaldehyde, equivalent to 0.15 mg formaldehyde/patch	polyvidone
22	Mercapto Mix, equivalent to 0.061 mg mercapto mix/patch	polyvidone
23	Thimerosal, equivalent to 0.0085 mg thimerosal/patch	hydroxypropyl cellulose
24	Thiuram Mix, equivalent to 0.020 mg thiuram mix/patch	polyvidone

The film-forming polymer which contains each allergen or allergen mix therein forms a dry film and is capable of adsorbing moisture from the tested skin area to swell to a gel when the patch is in use.

Further details of the approved product are set forth in the FDA approved package insert, a copy of which is submitted herewith in Appendix B.

U.S. Patent No. 4,836,217

**II. IDENTIFICATION OF FEDERAL STATUTE UNDER WHICH REGULATORY REVIEW OCCURRED**

Regulatory review of the approved product was conducted under Section 351 of the Public Health Service Act, Section 502 of the Federal Food, Drug, and Cosmetic Act and Title 21 Code of Federal Regulations, Part 600. The regulatory review was carried out by the Center of Biologics Evaluation and Research, Food and Drug Administration.

**III. DATE OF PERMISSION**

The product received permission for commercial marketing under the above-noted statutes on November 21, 1994.

**VI. IDENTIFICATION OF ACTIVE INGREDIENTS**

According to 35 USC 156(f), the term product means the active ingredient of, inter alia, a human biological product, including any salt or ester of the active ingredient as a single entity or in combination with another active ingredient. Accordingly, for the purposes of this application, Applicant submits that the active ingredient of the present drug product is the combination of active ingredients included in the 24 patches contained in the Allergen Patch Test product, as follows:

U.S. Patent No. 4,836,217

Panel 1

<u>Patch No.</u>	<u>Allergen or Allergen Mix</u>
1	Nickel sulfate, hexahydrate, equivalent to 0.036 mg nickel/patch
2	Wool alcohols, equivalent to 0.81 mg wool alcohols/patch
3	Neomycin sulfate, equivalent to 0.19 mg neomycin sulfate/patch
4	Potassium dichromate, equivalent to 0.0067 mg chromium/patch
5	Caine Mix, equivalent to 0.49 mg caine mix/patch
6	Fragrance Mix, equivalent to 0.35 mg fragrance mix/patch
7	Colophony, equivalent to 0.69 mg colophony/patch
8	Epoxy resin, equivalent to 0.032 mg diglycidylether of bisphenol-A/patch
9	Quinoline mix, equivalent to 0.154 mg quinoline mix/patch
10	Balsam of Peru, equivalent to 0.65 mg Balsam of Peru/patch
11	Ethylenediamine dihydrochloride, equivalent to 0.018 mg ethylenediamine/patch
12	Cobalt dichloride, equivalent to 0.0040 mg cobalt/patch

Panel 2

<u>Patch No.</u>	<u>Allergen or Allergen Mix</u>
13	p-tert Butylphenol formaldehyde resin, equivalent to 0.032 mg p-tert butylphenol formaldehyde/patch

U.S. Patent No. 4,836,217

- |    |  |
|----|--|
| 14 | Paraben Mix, equivalent to 0.81 mg paraben mix/patch                       |
| 15 | Carba Mix, equivalent to 0.20 carba mix/patch                              |
| 16 | Black Rubber Mix, equivalent to 0.061 mg black rubber mix/patch            |
| 17 | Cl+Me-Isothiazolinone, equivalent to 0.0032 mg Cl+Me-Isothiazolinone/patch |
| 18 | Quaternium-15, equivalent to 0.081 mg quaternium-15/patch                  |
| 19 | Mercaptobenzothiazole, equivalent to 0.061 mg mercaptobenzothiazole/patch  |
| 20 | p-Phenylenediamine, equivalent to 0.073 mg p-phenylenediamine/patch        |
| 21 | Formaldehyde, equivalent to 0.15 mg formaldehyde/patch                     |
| 22 | Mercapto Mix, equivalent to 0.061 mg mercapto mix/patch                    |
| 23 | Thimerosal, equivalent to 0.0065 mg thimerosal/patch                       |
| 24 | Thiuram Mix, equivalent to 0.020 mg thiuram mix/patch                      |

To the best of Applicant's knowledge, Applicant believes that this drug product containing the combination of active ingredients from the 24 patches has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act or the Virus-Serum-Toxin Act.

U.S. Patent No. 4,836,217

**V. APPLICATION SUBMITTED WITHIN 60-DAY PERIOD**

The present application is being submitted within the 60-day period permitted for submission pursuant to 37 CFR 1.720(f), which period expires after January 20, 1995.

**VI. PATENT FOR WHICH EXTENSION IS SOUGHT**

The patent for which a term extension is sought is the Fischer U.S. Patent No. 4,836,217 issued June 6, 1989. This patent is currently set to expire June 6, 2006.

**VII. COPY OF PATENT**

A copy of the Fischer U.S. Patent No. 4,836,217 is provided in Appendix C.

**VIII. DISCLAIMER, CERTIFICATION OF CORRECTION, RECEIPT OF MAINTENANCE FEE PAYMENT OR REEXAMINATION CERTIFICATE**

No Disclaimer, Certification of Correction or Reexamination Certificate has been issued in the Fischer U.S. Patent No. 4,836,217. A copy of the receipt for payment of the maintenance fee made September 24, 1992 is submitted herewith in Appendix D. The receipt is entitled Maintenance Fee Statement and is dated October 28, 1992.



U.S. Patent No. 4,836,217

**IX. THE PATENT CLAIMS THE APPROVED PRODUCT**

The Fischer U.S. Patent No. 4,836,217 contains 12 claims as set forth below. For convenience, the corresponding elements of the Allergen Patch Test are set forth adjacent the corresponding claim recitation.

CLAIMS	ELEMENTS OF APPROVED PRODUCT
1. In a test strip having at least one patch thereon and intended for use in occlusive epicutaneous testing in order to detect contact allergy, the improvement comprising that a dry film is adhered to one surface of said patch, said film containing as the film-forming substance a film-forming polymer which has incorporated therein a contact allergy test substance and said film-forming polymer being capable of adsorbing moisture from the tested skin area when the test strip is in use.	2 test strips containing a total of 24 patches  Each patch comprises a dry film of film-forming polymer which contains an allergen or an allergen mix and is capable of adsorbing moisture from tested skin area
2. A test strip according to claim 1 wherein said test strip contains a plurality of said patches.	24 patches
3. A test strip according to claim 2 wherein said hydrophilic film-forming polymer on at least one of said plurality of patches exhibits multiple alcoholic groups, or is a hydrophilic film-forming derivative thereof.	hydroxypropyl cellulose (patches 1, 4, 6-9, 12, 13, 15, 18, 23)  methylcellulose (patches 3, 11)
4. A test strip according to claim 2 wherein the contact allergy test substance on at least one of said plurality of patches is a metal salt.	Nickel sulfate (patch 1)
5. A test strip according to claim 2 wherein said film-forming polymer on at least one of the said plurality of patches is selected from methylated and hydroxy-propylated celluloses and mixture thereof.	hydroxypropyl cellulose (patches 1, 4, 6-9, 12, 13, 15, 18, 23)  methylcellulose (patches 3, 11)

U.S. Patent No. 4,836,217

CLAIMS	ELEMENTS OF APPROVED PRODUCT
6. A test strip according to claim 2 wherein said film on at least one of said plurality of patches comprises a methylated cellulose.	Patches 3, 11
7. A test strip according to claim 2 wherein said film on at least one of said plurality of patches comprises a hydroxy propylated cellulose.	Patches 1, 4, 6-9, 12, 13, 15, 18, 23
8. A test strip according to claim 1 wherein the area of said at least one patch is within the range of 0.2-4 cm <sup>2</sup> .	Each patch has an area of 0.81 cm <sup>2</sup>
9. A test strip according to claim 1 wherein the thickness of said film is less than 0.25 mm.	Each film has a thickness of 3 micrometers ( $\mu$ m)
10. A test strip according to claim 1 wherein the thickness of said film is less than 10.0 mm.	Each film has a thickness of 3 micrometers ( $\mu$ m)
11. A test strip according to claim 1 wherein said film consists of at least one hydrophilic film-forming polymer.	hydroxypropyl cellulose (patches 1, 4, 7-9, 12, 13, 15, 18, 23) methylcellulose (patches 3, 11)
12. A test strip according to claim 1 wherein said film-forming polymer adsorbs moisture from the tested skin area it swells to a gel.	all film-forming polymers employed swell to a gel on adsorption of moisture

U.S. Patent No. 4,836,217.

X. RELEVANT DATES PURSUANT TO 35 USC 156(g)

The Investigational New Drug Application was filed September 10, 1986 and was assigned IND No. BB-IND 2466, whereby the exemption became effective October 10, 1986. The original Product License Application for original Panel 1 of the Allergen Patch Test was filed July 16, 1986 and assigned PLA No. 86-0404. The Supplemental Product License Application for amended Panel 1 and Panel 2 of the Allergen Patch Test was filed February 26, 1991 and assigned PLA No. 91-0118. The Product License for the two panel Allergen Patch Test was approved November 21, 1994.

U.S. Patent No. 4,836,217

**XI. ACTIVITIES UNDERTAKEN BY APPLICANT DURING THE REGULATORY REVIEW PERIOD**

Set forth herein is a brief description of the significant activities undertaken by Pharmacia AB, including activities of its predecessors and licensee, during the regulatory review period with respect to the approved product. More specifically, the original Product License Application was filed by Pharmacia AB in 1986. In 1991, Pharmacia AB changed its name to Pharmacia Biosystems AB and the exclusive license rights of the invention of the Fischer U.S. Patent No. 4,836,217 were transferred to Kabi Vitrum AB. Kabi Vitrum AB then changed its name to Kabi Pharmacia AB. In 1993, Procordia AB changed its name to Pharmacia AB and in 1994, Kabi Pharmacia AB merged into Pharmacia AB derived from Procordia AB. Finally, Glaxo is a sublicensee of the invention of the Fischer U.S. Patent No. 4,836,217.

In the following description of activities, actions taken by the original Pharmacia AB, Kabi Vitrum AB, Kabi Pharmacia AB, the new Pharmacia AB and Glaxo during the regulatory review period are referred to as actions by "Pharmacia" in order to avoid confusion.

DATE	ACTIVITY
July 16, 1986	Product License Application for manufacture and sale of original Panel 1 of the Allergen Patch Test was submitted by Pharmacia to the FDA (PLA No. 86-0404).
September 10, 1986	Pharmacia submitted Investigational New Drug Application to the FDA (IND No. BB-IND 2466).

U.S. Patent No. 4,836,217

DATE	ACTIVITY
September 14-15, 1986	A meeting was conducted in Copenhagen, Denmark between Pharmacia personnel and Dr. Harold Bear, FDA, chairman of the Review Committee.
October 10, 1986	Exemption for Investigational New Drug Application becomes effective.
October 23, 1986	The product was presented by Pharmacia personnel to the FDA's Allergenic Products Advisory Board Committee in Washington.
December 22, 1986	A letter was sent from Pharmacia to the FDA discussing the clinical studies.
January 30, 1987	Pharmacia received a letter from the FDA concerning questions on chemical analytical methods.
August 16, 1987	Pharmacia responded to the FDA letter of January 30, 1987.
April 22, 1987	Pharmacia submitted to the FDA the results of clinical studies as requested by the FDA.
June 9, 1987	Pharmacia sent a letter to the FDA concerning specifications and stability issues.
June 22, 1987	A meeting was conducted in Washington between the FDA and Pharmacia personnel. Discussions related to chemistry, clinical documentation and a package insert.
July 28, 1987	A meeting was conducted with Pharmacia personnel and FDA representatives in Uppsala, Sweden in relation to an FDA inspection of the manufacturing facilities.
September 4, 1987	Pharmacia submitted to the FDA chemical data and answers related to meetings with the FDA on June 22 and July 28, 1987, as well as a revised draft of the package insert.
November 3, 1987	Pharmacia submitted to the FDA a protocol on a post-approval clinical trial.
February 2, 1988	Pharmacia was issued a letter from the FDA concerning specifications and analytical methods.
March 24, 1988	Pharmacia submitted answers to the FDA letter of February 2, 1988.

U.S. Patent No. 4,836,217

DATE	ACTIVITY
March 30, 1988	Pharmacia submitted a report to the FDA on clinical studies as requested by the FDA.
May 23-25, 1988	Meetings were conducted in Washington between Pharmacia personnel and the FDA, including the Allergy Advisory Board and individual FDA representatives.
June 22, 1988 July 21, 1988	Pharmacia submitted analytical data to the FDA.
September 29, 1988	Pharmacia submitted a regulatory report to the FDA covering chemical and clinical questions discussed with the FDA during previous meetings and several telephone conversations.
November 7, 1988	Pharmacia submitted a response to an undated fax from the FDA received at the beginning of October 1988.
November 9, 1988	Pharmacia was issued a letter from the FDA concerning outstanding issues for the product license application.
November 18, 1988	Pharmacia submitted analytical Standard Operating Procedures and a process validation report.
December 12, 1988	A meeting was conducted between Pharmacia personnel and the FDA in Washington concerning labelling, stability, microbiology and batch release.
February 10, 1989	Pharmacia submitted answers to questions raised during the meeting on December 12, 1988.
March 9, 1989	Pharmacia was issued a letter from the FDA concerning specifications, shipment, name issues and clinical studies.
April 7, 1989	Pharmacia submitted to the FDA answers to the March 9, 1989 letter.
April 17, 1989	Pharmacia submitted to the FDA four analytical Standard Operating Procedures.
May 30, 1989	Pharmacia was issued the FDA comments to the Pharmacia submission of November 18, 1988.
June 28, 1989	Pharmacia submitted to the FDA its response to the FDA letter of May 30, 1989.

U.S. Patent No. 4,836,217

DATE	ACTIVITY
August 29, 1989	Pharmacia was issued a response from the FDA relating to the submissions of February 10, April 7, and April 17, 1989 as well as questions raised during the December 12, 1988 meeting and by the FDA letter of March 9, 1989.
September 6, 1989	Pharmacia responded to the FDA letter of August 29, 1989.
November 1, 1989	Pharmacia submitted a draft of the Summary of Basis of Approval.
February 7, 1990	Pharmacia submitted a revised draft package insert and suggested post-approval commitments.
April 18, 1990	Package insert for original Panel 1 was approved by the FDA.
July 13, 1990	The FDA approved Panel 1 with 11 allergens and one negative control patch for manufacture and use.
February 26, 1991	A supplement to the original Product License Application, containing Panel 2 and a modified Panel 1 was submitted by Pharmacia to the FDA (PLA No. 91-0118).
November 26, 1991	Pharmacia was issued questions from the FDA relative to the submission of February 26, 1991.
December 5, 1991	A meeting was conducted between Pharmacia personnel and the FDA concerning the November 26, 1991 letter and other issues.
February 10, 1992	Pharmacia submitted to the FDA answers to the FDA letter of November 26, 1991.
October 29, 1992	A meeting was conducted between Pharmacia personnel and the FDA concerning stability, batch release issues and clinical studies.
December 4, 1992	Pharmacia submitted to the FDA additional stability data and suggestions for the transport simulation protocol.
January 7 & 19, 1993 February 10 & 17, 1993	Pharmacia submitted to the FDA several clinical reports.
February 24, 1993	Pharmacia submitted to the FDA current analytical specifications.

U.S. Patent No. 4,836,217

DATE	ACTIVITY
March 5, 1993	Pharmacia submitted to the FDA answers to various questions raised during a phone conversation with the FDA.
April 30, 1993	A meeting was conducted between Pharmacia personnel and the FDA on outstanding issues for approval of the product containing two panels.
July 8, 1993	Pharmacia submitted to the FDA a first draft of the package insert for the product containing two panels.
July 18-20, 1993	Meetings were conducted between Pharmacia personnel and the FDA, including the Allergic Extracts Advisory Committee.
July 22, 1993	Pharmacia submitted draft labelling for the product cartons and foil.
July 29, 1993	Pharmacia received comments from the FDA on the proposed carton and foil labelling.
August 12, 1993	Pharmacia resubmitted draft labelling for the product cartons and foil.
August 16, 1993	Pharmacia received questions from the FDA on the clinical studies submitted earlier in 1993.
September 3, 1993	Pharmacia submitted a response to the FDA answering the questions on the clinical studies.
September 23, 1993	The resubmitted proposed product cartons and foil labelling were approved by the FDA.
October 7, 1993	Pharmacia received comments from the FDA on the first draft of the package insert which was submitted July 8, 1993.
November 2, 1993	The Establishment License Application was approved.
November 4, 1993	A meeting was conducted between Pharmacia personnel and the FDA to discuss issues.
November 12, 1993	Pharmacia submitted to the FDA a second draft of the package insert and a draft of an annotated package insert.
December 3, 1993	Pharmacia submitted to the FDA additional information on the clinical questions raised August 16, 1993.
December 23, 1993	Pharmacia received from the FDA comments on the second draft of the package insert.



U.S. Patent No. 4,836,217

DATE	ACTIVITY
January 20, 1994	Pharmacia submitted to the FDA a third draft of a package insert for the two panel product.
February 23, 1994	Pharmacia submitted a post-approval commitment proposal to the FDA.
February 24, 1994	Pharmacia submitted a draft summary basis for approval to the FDA and received from the FDA comments on the third draft of the package insert for the two panel product.
February 28, 1994	Pharmacia submitted a fourth draft of the package insert for the two panel product.
March 13, 1994	Pharmacia received comments from the FDA on the fourth draft of the package insert for the two panel product.
March 18, 1994	Pharmacia submitted to the FDA a fifth draft of the package insert for the two panel product.
May 10, 1994	Pharmacia received comments from the FDA on the annotated package insert for the two panel product which had been submitted February 23, 1994.
May 17, 1994	Pharmacia submitted a response to the FDA comments on the annotated package insert.
May 31, 1994	Pharmacia was issued a request for reference information from the FDA.
June 3, 1994	Pharmacia submitted a response to the FDA request of May 31.
June 10, 1994	Pharmacia received clinical questions from the FDA.
June 17, 1994	Pharmacia submitted a response to the FDA to the clinical questions received June 10.
June 21, 1994	Pharmacia submitted a sixth draft of the package insert for the two panel product.
June 28, 1994	Pharmacia received comments from the FDA on the consultant's comments of the package insert.
June 30, 1994	Pharmacia received clinical questions from the FDA.
July 6, 1994	Pharmacia submitted a response to the FDA to the clinical questions received June 30, 1994.

U.S. Patent No. 4,836,217

DATE	ACTIVITY
July 6, 1994	Pharmacia received comments from the FDA on the sixth draft of the package insert for the two panel product.
July 7, 1994	Pharmacia received further comments from the FDA on the package insert.
July 11, 1994	Pharmacia submitted a seventh draft of the package insert for the two panel product and responded to comments received July 7, 1994.
July 14, 1994	Pharmacia received consultant's comments from the FDA on the toxicology section of the package insert.
July 18, 1994	Pharmacia submitted a response to the FDA to the toxicology questions.
July 21, 1994	Pharmacia received a request from the FDA for additional toxicology information in the package insert for the two panel product and Pharmacia submitted the eighth draft of the package insert to the FDA.
July 22, 1994	Pharmacia received a request from the FDA to add bioequivalence data to the package insert.
July 25, 1994	Pharmacia submitted the ninth draft of the package insert to the FDA. Pharmacia also received comments from the FDA on the post-approval commitment proposal submitted February 23.
July 27, 1994	Pharmacia responded to the comments on the post-approval commitments from the FDA.
July 28, 1994	Pharmacia received a change to the post-approval commitments from the FDA.
August 2, 1994	Pharmacia agreed to the change in the post-approval commitments with the FDA.
November 21, 1994	Pharmacia received the approval for the two panel product.

U.S. Patent No. 4,836,217

XII. ELIGIBILITY AND LENGTH OF EXTENSION

A. ELIGIBILITY

In the opinion of the Applicant, Pharmacia AB, the Fischer U.S. Patent No. 4,836,217 is eligible for extension. Namely, in accordance with the provisions of 35 USC 156(a) and 37 CFR 1.720:

(a) The patent claims a product, namely a human biological product, comprising a 2 panel test strip;

(b) The term of the Fischer U.S. Patent No. 4,836,217 will not expire before submission of the present application;

(c) The term of the Fischer U.S. Patent No. 4,836,217 has never been extended;

(d) The present application for extension is submitted by the agent, Pharmacia AB, for the owner of record of the patent, Dr. Torkel Fischer, and in compliance with 35 USC 156(d) and 37 CFR 1.740;

(e) The 2 panel test strip product has been subject to a regulatory review period before its commercial marketing or use; and

(f) The permission for the commercial marketing or use of the 2 panel test strip product after the regulatory review period is the first permitted commercial marketing or use of the 2 panel test strip product under the provision of law under which the regulatory review period occurred.

U.S. Patent No. 4,836,217

B. LENGTH OF EXTENSION

The length of the extension claimed is 898 days, whereby the term of the Fischer U.S. Patent No. 4, 836,217 would be extended to November 21, 2008. The length of extension was determined as set forth in the calculation of length of patent term extension for a human drug product form set forth in Appendix E, and as follows:

(a) There was no regulatory review period as defined by 35 USC 156(g)(1)(B)(i) since an investigational new drug application was filed September 10, 1986 and the exemption became effective October 10, 1986, but the original product license application was filed earlier, namely July 16, 1986. Accordingly, the number of days in the period as set forth in 37 CFR 1.775(c)(1) is zero days.

(b) The regulatory review period defined by 35 USC 156(g)(1)(B)(ii) ran from July 16, 1986 to November 21, 1994 whereby the number of days in the period set forth in 37 CFR 1.775(c)(2) is 3,050 days.

(c) Accordingly, the length of the regulatory review period defined by 37 CFR 1.775(c) is 3,050 days.

(d) According to 37 CFR 1.775(d)(1)(i), the period of 3,050 days is reduced by the number of days which were on or before the date on which the patent issued, namely from July 16, 1986 to June 6, 1989 for a total of 1,055 days, whereby the length of the regulatory review period remaining according to 37 CFR 1.775(d)(1)(i) is 1,995 days.

U.S. Patent No. 4,836,217

(e) According to 37 CFR 1.775(d)(1)(ii), the regulatory review period is also reduced by the number of days in which it is determined that the Applicant did not act with due diligence. Applicant submits that this is zero days, whereby the length of the regulatory review period remaining according to 37 CFR 1.775(d)(1)(ii) is 1,995 days.

(f) According to 37 CFR 1.775(d)(1)(iii), the regulatory review period is also reduced by one-half the number of days in the period defined by 37 CFR 1.775(c)(1) after that period is reduced by the number of days in the regulatory review period on and before the date on which the patent issued and the number of days in the periods that Applicant did not act with due diligence. Since the period defined by paragraph (c)(1) of 37 CFR 1.775 is zero, the length of the period remaining according to 37 CFR 1.775(d)(1)(iii) is 1,995 days.

(g) According to 37 CFR 1.775(d)(2), addition of 1,995 days to the original expiration date of the Fischer U.S. Patent No. 4,836,217 provides an expiration date of November 22, 2011.

(h) According to 37 CFR 1.775(d)(3), addition of 14 years to the date of approval of the application, namely November 21, 1994, results in a date of November 21, 2008. Under 37 CFR 1.775(d)(4), this date of November 21, 2008 is earlier than the date noted in paragraph (g) set forth above and is therefore selected.

U.S. Patent No. 4,836,217

(i) According to 37 CFR 1.775(d)(5)(1), addition of five years to the original expiration date of the Fischer U.S. Patent No. 4,836,217 provides a date of June 6, 2011, which is later than the date of November 21, 2008 noted in paragraph (h) set forth above, whereby under 37 CFR 1.775(d)(5)(ii), November 21, 2008 is selected as the date to which the term of the patent is extended, whereby the term of the patent is extended for a total of 898 days.

**XIII. DUTY TO DISCLOSE**

Applicant Pharmacia AB acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought, including as set forth in 37 CFR 1.765.

**XIV. APPLICATION FEE**

Please charge the Government Fee of \$1,030.00 for Application for Extension of Patent Term to Deposit Account No. 12-2237. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 12-2237 and please credit any excess fees to such deposit account.

U.S. Patent No. 4,836,217

**IV. INQUIRIES AND CORRESPONDENCE**

Inquiries and correspondence relating to the present  
Application for Patent Term Extension should be directed to:

Holly D. Kozlowski, Esq.  
LOWE, PRICE, LEBLANC & BECKER  
99 Canal Center Plaza, Suite 300  
Alexandria, VA 22314  
703-684-1111

U.S. Patent No. 4,836,217

**XVI. DECLARATION**

This application is submitted for extension of the term of the Fischer U.S. Patent No. 4,836,217. The undersigned, as agent for both the patent owner, Dr. Torkel Fischer, and his agent, Pharmacia AB, hereby declares that:

(1) She is a patent attorney authorized to practice before the U.S. Patent and Trademark Office and has general authority from Pharmacia AB, the agent of the Dr. Torkel Fischer, and Dr. Torkel Fischer, the owner of the Fischer U.S. Patent No. 4,836,217, to act on behalf of the agent and owner in patent matters;

(2) She has reviewed and understands the contents of the attached application papers for patent term extension consisting of 25 pages of application and Appendices A-E submitted pursuant to 35 USC 156 and 37 CFR 1.740;

(3) She believes that the Fischer U.S. Patent No. 4,836,217 is subject to extension pursuant to 37 CFR 1.710;

(4) She believes an extension of the length claimed is justified under 35 USC 156 and the applicable regulations; and

(5) She believes the patent for which the extension is being sought meets the conditions for the extension of the term of patent as set forth in 37 CFR 1.720.

The undersigned further declares that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and further that



U.S. Patent No. 4,836,217

these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent extension issuing thereon.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 12-2237 and please credit any excess fees to such deposit account.

Respectfully submitted,

LOWE, PRICE, LEBLANC & BECKER



Holly D. Kojowski  
Registration No. 30,468

99 Canal Center Plaza, Suite 300  
Alexandria, Virginia 22314  
(703) 684-1111 HDK:abj  
Date: January 20, 1995



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

FEB 14 1995

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

#29

Dear Mr. Wilson:

The enclosed application for extension of the patent term of U.S. Patent No. 4,836,217 issued on June 6, 1989, was filed on January 20, 1995, under 35 USC § 156.

Your assistance is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC § 156(g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 USC § 156(d)(2)(A).

Our review of the application to date indicates that the subject matter would be eligible for extension of the patent term under 35 USC § 156.

Gerald A. Dost  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

(703) 305-9285

cc: Holly D. Kozlowski, Esq.  
Lowe, Price, Leblanc & Becker  
99 Canal Center Plaza, Suite 300  
Alexandria, VA 22314



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20867

JUN 21 1995

Re: Allergen Patch Test (Thin-layer Rapid Use  
Epicutaneous (T.R.U.E.) Test)  
Docket No. 95B-0047

430

Stephen G. Kunin  
Deputy Assistant Commissioner for  
Patent Policy and Projects  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

RECEIVED  
JUN 23 1995  
OFFICE OF THE ASSISTANT  
COMMISSIONER FOR PATENTS

Dear Mr. Kunin:

This is in regard to the application for patent term extension for U.S. Patent No. 4,836,217 filed by Pharmacia under 35 U.S.C. § 156. The human drug product claimed by the patent is Allergen Patch Test (Thin-layer Rapid Use Epicutaneous (T.R.U.E.) Test), which was assigned Product License Application (NDA) No. 91-0118.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product.

The PLA was approved on November 21, 1994, which makes the submission of the patent term extension application on January 20, 1995, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Holly D. Kozlowski, Esq  
Lowe, Price, LeBlanc & Becker  
99 Canal Center Plaza, Suite 300  
Alexandria, VA 22314



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

APR 16 1996

#34

Holly D. Kozlowski, Esq.  
Lowe, Price, LeBlanc & Becker  
99 Canal Center Plaza, Suite 300  
Alexandria, VA 22314

Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,836,217

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,836,217, which issued June 6, 1989 and which claims the medical device Allergen Patch Test (Thin-layer Rapid Use Epicutaneous (T.R.U.E.) Test), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 899 days.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of August 3, 1995 (60 Fed. Reg. 39,752). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= 1/2 \text{ (Testing Phase) + Approval Phase} \\ &= 1/2 (1,601 - 970) + 1,365 \\ &= 1,681 \text{ days}\end{aligned}$$

Since the regulatory review period began October 10, 1986, before the patent issued (June 6, 1989), only that portion of the regulatory review period occurring after the date the patent issued has been considered in the above determination of the length of the extension period 35 U.S.C. § 156(c). (From October 10, 1986 to June 6, 1989 is 970 days; this period is subtracted for the number of days occurring in the testing phase according to the FDA determination of the length of the regulatory review period:  $1,601 - 970 = 631$  days.) No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The 14 year exception of 35 U.S.C. § 156(c)(3) operates to limit the term of the extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the approved product (November 21, 1994) when added to the period of extension calculated above (1,681 days) cannot exceed fourteen years. The period of extension is thus limited to November 21, 2008, by operation of 35 U.S.C. § 156(c)(3). Since the patent term of seventeen years (35 U.S.C. § 154)<sup>1</sup> would

<sup>1</sup> 35 U.S.C. § 154 was amended by the Uruguay Round Agreements Act to provide, in subsection (c)(1) thereof, that a patent in force on June 8, 1995 shall have the longer term of

expire on June 6, 2006, the period of extension is the number of days to extend the term of the patent from its expiration date to and including November 21, 2008, or 899 days.

The limitations of 35 U.S.C. § 156(g)(6) do not operate to further reduce the period of extension determined above.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Commissioner will issue a certificate of extension, under seal, for a period of 899 days.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.:	4,836,217
Granted:	June 6, 1989
Applicant:	Torkel I. Fischer
Owner of Record:	Pharmacia AB
Title:	Hypersensitivity Test Means
Classification:	128/743
Product Trade Name:	Allergen Patch Test (Thin-layer Rapid Use Epicutaneous (T.R.U.E.) Test)
Term Extended:	899 days

seventeen years from the issue date or 20 years from the filing date of the application or an earlier filed application to which a specific reference is made under 35 U.S.C. § 120, 121 or 365(c). The application that resulted in U.S. Patent No. 4,836,217 was a national stage application of a Patent Cooperation Treaty Application that was filed on September 23, 1985. Thus, the application contained a specific reference to an earlier application under 35 U.S.C. § 365(c) and 20 years from that date would have been, September 23, 2005, which is before June 6, 2007, the expiration of the original seventeen year term. Since the original seventeen year term is longer than the new term defined by the amendment to § 154, it is unnecessary to determine whether the patent term extension can be added to the new term.

U.S. Patent No. 4,836,217

3

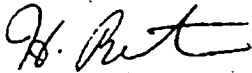
Any correspondence with respect to this matter from the applicant should be addressed as follows:

By mail: Assistant Commissioner for Patents  
Box DAC  
Washington, D.C. 20231

By FAX: (703) 308-6916  
Attn: Special Program Law Office

By hand: One Crystal Park, Suite 520  
2011 Crystal Drive  
Arlington, VA

Telephone inquiries should be directed to Karin Tyson at (703) 305-9285.



Hiram H. Bernstein  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

(703) 305-9285

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 11-44  
Rockville, MD 20857

RE: Allergen Patch Test (Thin-layer  
Rapid Use Epicutaneous (T.R.U.E.) Test)  
FDA Docket No.: 95E-0047

1

#35

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

PATENT NO. : 4,836,217  
ISSUED : June 6, 1989  
INVENTOR(S) : Torkel I. Fischer  
PATENT OWNER : Pharmacia AB

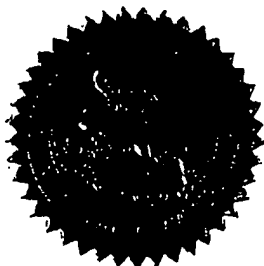
This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

899 days

from the original expiration date of the patent, June 6, 2006, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 31st day of May 1996.

*Bruce A. Lehman*

Bruce A. Lehman  
Assistant Secretary of Commerce and  
Commissioner of Patents and Trademarks



AVANIR.000GEN

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of : KATZ, David H. )  
Group Art Unit 125 )  
Appl. No. : 07/345,084 )  
Filed : April 28, 1989 )  
Patent No. : U. S. Patent No. 4,874,794 )  
Issued : October 17, 1989 )  
For : INFLAMMATORY DISEASE )  
TREATMENT )  
Examiner : FRIEDMAN, Stanley J. )

RECEIVED

SEP 27 2000

OFFICE OF PETITIONS

**APPLICATION FOR EXTENSION OF PATENT TERM BASED ON  
REGULATORY REVIEW OF A NEW DRUG APPLICATION  
PURSUANT TO 35 U.S.C. § 156**

Assistant Commissioner for Patents  
Washington, D.C. 20231  
Box: Patent Ext.

Dear Sir:

The Applicant, AVANIR Pharmaceuticals, of 11388 Sorrento Valley Road, San Diego, CA 92121, represents that it is the owner of record of the entire right, title and interest in and to U. S. Patent No. 4,874,794, as evidenced by the Assignments from the Inventor to LIDAK PHARMACEUTICALS recorded on April 6, 1990 under Reel/Frame: 5293/0061, and the later Assignment from LIDAK PHARMACEUTICALS to AVANIR PHARMACEUTICALS recorded on April 20, 1999 under Reel/Frame: 9901/0274. The recorded Assignments along with the two Notice of Recordation of Assignment Documents, copies of which are submitted as **Exhibit A**, refer specifically to Patent Application Serial No. 07/345,084, filed on April 28, 1989, and U.S. Patent No. 4,874,794 issued on October 17, 1989. The recorded Assignments assign the full and exclusive right, title and interest in and to the invention disclosed in Patent Application Serial No. 07/345,084, from which U.S. Patent No. 4,874,794 was granted.



**Patent No** : U.S. 4,874,794  
**Issued** : October 17, 1989

AVANIR Pharmaceuticals hereby applies, pursuant to 35 U.S.C. § 156 (d) (1) and 37 C.F.R. § 1.740, for extension of the term of the above-identified U. S. Patent No. 4,874,794 issued on October 17, 1989, and based on U. S. Application Serial No. 07/345,084 filed on April 28, 1989.

U. S. Patent No. 4,874,794 results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act (December 8, 1994), accordingly, its date of expiration under 35 U.S.C. § 154 (c) (1) is April 28, 2009, the greater of the 20-year term from the filing date (April 28, 1989), or 17 years from grant (October 17, 2006).

The patent term extension is requested until April 28, 2014, five years (1826 days) from the original expiration date, or such greater or lesser period as the Commissioner may deem AVANIR Pharmaceuticals to be entitled. This is the maximum permitted extension provided in 35 U.S.C. § 156. The regulatory review period (reduced by one-half of the IND period) is 2124 days, which is greater than either 14 years from the date of approval (July 25, 2014) provided in 37 C.F.R. §1.775(d)(3) or 5 years from the original expiration date (April 28, 2014) provided in 37 C.F.R. §1.775(d)(5)(i).

This application for patent term extension is based on the regulatory approval of Abreva™. The sole active ingredient in Abreva™ is 10% docosanol, a 22-carbon aliphatic alcohol.

Docosanol is produced by high-pressure hydrogenation of erucic acid, an unsaturated, 22-carbon fatty acid. Hydrogenation of erucic acid is carried out in the presence of fine-grained, slurried copper-chromite catalyst at a temperature and pressure of approximately 285° C and 300 bar, respectively. Crude *n*-docosanol is purified by multi-step, fractional distillation. Then it is processed through a post-hydrogenation plant containing a fixed-bed nickel catalyst to remove any C-22 aldehyde, which might be present in the crude material.

A method of using 10% docosanol, the active ingredient in Abreva™, for treating virus-induced and inflammatory diseases is claimed in U. S. Patent No. 4,874,794.

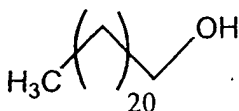
The date of the NDA approval of Abreva™ is July 25, 2000. This is the first permitted commercial marketing or use of this active ingredient as a human drug product. This application is accordingly being made within the 60-day statutory period provided in 35 U.S.C. § 156(d).

**Patent No** : U.S. 4,874,794  
**Issued** : October 17, 1989

In accordance with 37 C.F.R. § 1.740, AVANIR Pharmaceuticals provides the following information:

- (1) *A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics.*

AVANIR Pharmaceuticals submits herewith as **Exhibit B** to this application the prescribing information for Abreva™ as approved by the U. S. Food and Drug Administration (FDA). *n*-Docosanol, the sole active ingredient in Abreva™, is an aliphatic alcohol, commonly known as benenyl alcohol, which is a white waxy solid having a melting point of between 70° and 72° C. It has the molecular formula C<sub>22</sub>H<sub>46</sub>O and a molecular weight of 326.61. The structure of *n*-docosanol is:



- (2) *A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred.*

The regulatory review was conducted under Sec. 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355), pursuant to the regulations set forth in 21 C.F.R. 314.

- (3) *An identification of the date on which the product received permission for commercial marketing or use under the provisions of law under which the applicable regulatory review period occurred.*

The approved product received permission for commercial marketing or use under Sec. 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355) on July 25, 2000. A copy of the approval letter received from the FDA is attached as **Exhibit C**.

- (4) *An identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone*

Patent No : U.S. 4,874,794  
Issued : October 17, 1989

*or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved.*

The active ingredient in Abreva™ is the above-described aliphatic alcohol (docosanol), which has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

- (5) *A statement that the application is being submitted within the sixty-day period permitted for submission pursuant to § 1.720(f) and an identification of the date of the last day on which the application could be submitted.*

This application is being submitted on or before September 25, the last day of the sixty-day period permitted for submission pursuant to 37 C.F.R. § 1.720(f), i.e. the last day of the sixty-day period following the July 25, 2000 approval for commercial marketing of Abreva™, that is not a Saturday, Sunday, or Federal holiday, as provided in 35 U.S.C. § 156 (d) (1); 37 C.F.R. § 1.720(f) and 37 C.F.R. § 1.7.

- (6) *A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration.*

This application seeks extension for U. S. Patent No. 4,874,794, issued to David H. KATZ on October 17, 1989. The patent will expire on April 28, 2009.

- (7) *A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings.*

A copy of U. S. Patent No. 4,874,794, including claims and drawings, is enclosed as **Exhibit D.**

- (8) *A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or reexamination certificate issued in the patent.*

Copies of the Maintenance Fee Statements for the first and second maintenance fee payments are enclosed as **Exhibit E.**

U. S. Patent No. 4,874,794 has not been subject to any disclaimer, certificate of correction, or reexamination.

Patent No : U.S. 4,874,794  
Issued : October 17, 1989

- (9) *A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or method of using or manufacturing the approved product.*

The approved product is the active ingredient in Abreva™, 10% docosanol. Claim 1 encompasses a method of using the approved product for treating virus-induced and inflammatory diseases of skin and membranes in humans or animals. The relationship between the Claim 1 of U. S. Patent No. 4,874,794 and methods of using the approved product is as follows:

<b>Claim 1.</b> A method treating virus-induced and inflammatory diseases of skin and membranes in humans or animals is recited, comprising topical application of a composition consisting of one or more of the aliphatic alcohols docosanol, tetraconsanol and hexacosanol in a concentration of from 0.1 to 25 percent by weight in a physiologically compatible carrier to the inflamed skin or membrane of the patient to be treated.	<b>Approved product and method of using:</b> Abreva™ (10% docosanol) was approved for treating cold sores (fever blisters), which are inflammatory skin conditions that may be induced by viral infection. Topical application of a composition consisting of 10% docosanol was approved in a physiologically compatible cream. Docosanol is one of the three aliphatic alcohols recited in Claim 1. The approved concentration of 10% is encompassed by the recited concentration range of from 0.1 to 25 percent by weight.
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Patent No : U.S. 4,874,794  
Issued : October 17, 1989

- (10) *A statement beginning on a new page, of the relevant dates and information pursuant to 35 U.S.C. 156 (g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period, particularly, for a patent claiming a human drug, antibiotic, or human biological product, the effective date of the investigational new drug (IND) application and the IND number; the date on which a new drug application (NDA) or a Product License Application (PLA) was initially submitted and the NDA or PLA number and the date on which the NDA was approved or the Product License issued.*

The following dates and related information are applicable for the new drug application (NDA) approval of Abreva™:

Date of IND:	July 11, 1991
IND Number:	37,321
Submission Date of NDA:	December 22, 1997 for acceptance of the completed NDA; a presubmission of drug substance, drug product and environmental assessment information, and nonclinical pharmacology, toxicology and pharmacokinetics was made on November 25, 1997.
FDA Approval Date for NDA:	July 25, 2000
NDA Number:	20-941

Patent No : U.S. 4,874,794  
Issued : October 17, 1989

- (11) *A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities.*

The regulatory review period began on July 11, 1991 with the submission of the IND. During the period beginning July 11, 1991, and continuing through July 25, 2000, efforts were underway by AVANIR Pharmaceuticals, the marketing applicant, to gain approval of the New Drug Application (NDA), which was filed in stages beginning November 25, 1997 and completed on December 22, 1997.

During this period, the following significant activities and dates are applicable:

Date	Activity
July 11, 1989	Submit IND.
August 26, 1991	Submit supplement (001) to IND application 37,321 with results of <i>in vitro</i> and <i>in vivo</i> studies of docosanol effects on HSV-1 and HSV-2 infection.
February 12, 1992	Letter to FDA (002) with additional data regarding pharmacology, toxicology and microbiology.
March 16, 1992	Letter to FDA (003) regarding information amendment with additional data regarding chemistry and microbiology.
April 2, 1992	Letter to FDA (004) with additional data regarding pharmacology, toxicology and clinical.
April 9, 1992	Letter to FDA (005) regarding new protocol for Phase II clinical investigation.
April 15, 1992	Letter to FDA (006) regarding amendment to Report of RCC.

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June 19, 1992	Letter to FDA (007) regarding Information amendment (chemistry/microbiology) and Protocol amendment (change in protocol).
July 15, 1992	Letter to FDA (008) regarding chemistry, manufacturing and controls.
September 17, 1992	Letter to FDA (009) regarding topical cream formulation.
September 25, 1992	Letter to FDA (010) regarding investigator's brochure and new protocol for Phase II clinical investigation.
October 6, 1992	Letter to FDA (011) regarding protocol amendment, information amendment, and response to FDA request for information.
November 6, 1992	Letter to FDA (012) regarding protocol amendment and Annual Report.
December, 1992 – June, 1993	Randomized, double-blind, steric acid placebo-controlled study (92-LID-02).
January 12, 1993	Letter to FDA (013) regarding Protocol amendment and Information amendment.
March 14, 1993 – March 6, 1995	Phase II, randomized, double-blind, steric acid placebo-controlled study (92-LID-04).
March 24, 1993	Letter to FDA (014) regarding change in protocol 92-LID-04, Information amendment, clinical protocol, IRB approval, and IRB approved consent form.
January 20, 1994	Letter to FDA (015) regarding Annual Report for 10% docosanol cream.
January 27, 1994	Letter to FDA (016) regarding amendment to 92-LID-03 and 92-LID-04, and amendment to information (chemistry/microbiology).
March, 1994 – March, 1995	Randomized, double-blind, docosanol vs. acyclovir 5% cream study (94-LID-01).
June 9, 1994	Letter to FDA (017) regarding overview of package and package for end of Phase II meeting, with formulation development history, ADME studies, toxicology studies, carcinogenicity rationale, Phase I safety studies, Phase II clinical studies and Phase III clinical program.
June 22, 1994	Letter to FDA (018) regarding complete protocols for toxicology and metabolic studies.

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July 5, 1994	Letter to FDA (019) regarding IRB approval, 94-LID-01 brochure/protocol, 92-LID-02 reports and completed acute toxicology studies.
July 13, 1994	Letter to FDA (020) regarding response to request for information.
August 2, 1994	Letter to FDA (021) regarding response to request for information.
September 7, 1994	Letter to FDA (022) regarding end of Phase II meeting minutes.
September 21, 1994	Letter to FDA (023) regarding revised protocols 92-LID-04 and new protocols 94-LID-01 and 94-LID-03; IRB approval.
September 23, 1994	Letter to FDA (024) regarding Adverse Events Report.
November 8, 1994	Letter to FDA (025) regarding revised protocols 94-LID-04 and 94-LID-05.
November 15, 1994	Letter to FDA (026) regarding regulatory status of Phase III protocols.
November 17, 1994	Letter to FDA (027) regarding transfer of monitoring responsibility to CRO.
December 5, 1994	Letter to FDA (028) regarding response to end of Phase II meeting pharm/tox issues and carcinogenicity testing.
December 8, 1994	Letter to FDA (029) regarding absorption of labeled docosanol in cream formula 3.
December 12, 1994 – August 17, 1995	Clinic-initiated, double-blind, steric acid placebo-controlled study (94-LID-04).
December 15, 1994 – October 27, 1995	Clinic-initiated, double-blind, steric acid placebo-controlled study (94-LID-05).
January 5, 1995	Letter to FDA (030) regarding new investigators.
January 30, 1995	Letter to FDA (031) regarding Annual Report.
February 14, 1995	Letter to FDA (032) regarding ADME and Toxicology Program for docosanol 10% cream.
March 8, 1995	Letter to FDA (033) regarding 92-LID-04 Safety report and 94-LID-04 & 05 new investigators.
May 4, 1995 – October 20, 1995	Clinic-initiated, double-blind, steric acid placebo-controlled study (95-LID-10).



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March 27, 1995	Letter to FDA (035) regarding new protocol 95-LID-10, amended protocols 94-LID-04 & 05, and summary of changes for 94-LID-04 & 05.
May 5, 1995	Letter to FDA (036) regarding new protocols, 95-LID-03a,b,c and completed toxicology study final report.
June 8, 1995	Letter to FDA (038) regarding 95-LID-10 new investigators and transfer to CRO and 95-LID-03a amended protocol
July 26, 1995	Letter to FDA (039) regarding amended protocols and summaries of changes for studies 95-LID-10, 94-LID-05 and 94-LID-04.
October 31, 1995	Letter to FDA (040) regarding Annual Report of docosanol 10% cream
November 21, 1995	Letter to FDA (041) regarding revised statistical sections for studies 95-LID-10, 94-LID-05 and 94-LID-04.
February 7, 1996	Letter to FDA (043) regarding final reports for LAK/015, 010, 009, 011, 013, 014 and 6634-100.
February 14, 1996	Letter to FDA (046) regarding demographic data for 95-LID-10, 94-LID-05, 94-LID-04 and 92-LID-04 studies.
March 5, 1996	Letter to FDA (047) regarding final reports for 95-LID-03a, b, and c.
April 10, 1996	Letter to FDA (048) regarding placebo formulation issues.
July 29, 1996 – April 21, 1997	Clinic-initiated, double-blind, placebo-controlled multicenter study to assess safety and efficacy of topical docosanol 10% cream (96-LID-06).
May 2, 1996	Letter to FDA (049) regarding IRB approval of 95-LID-KS and MC and amended protocols.
June 10, 1996	Letter to FDA (050) regarding new protocols 95-LID-KS2 and MC2.
June 19, 1996	Letter to FDA (053) regarding amended protocol 95-LID-KS and summary of changes.
July 31, 1996	Letter to FDA (055) regarding amended protocol 95-LID-06 and summary of changes.
August 15, 1996	Letter to FDA (056) regarding amended protocol 95-LID-07 and summary of changes, new investigators and glossary of terms.

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**Issued** : October 17, 1989

September 17, 1996	Letter to FDA (057) regarding modified consent forms.
October 14, 1996 – May 12, 1997	Clinic-initiated, double-blind, placebo-controlled multicenter study to assess safety and efficacy of topical docosanol 10% cream (96-LID-07).
October 18, 1996	Letter to FDA (058) regarding new investigators.
November 5, 1996	Letter to FDA (059) regarding IND safety reports for 95-LID-KS and MC.
December 10, 1996	Letter to FDA (060) regarding Annual Report.
December 20, 1996	Letter to FDA (061) regarding integrated clinical statistical report for 94-LID-04.
January 16, 1997	Letter to FDA (062) regarding studies LAK/006,012, 015, 018, 008, and 48B-L-20.
February 5, 1997	Letter to FDA (063) regarding integrated clinical statistical report for 94-LID-10.
February 21, 1997	Letter to FDA (064) regarding combined analysis of studies 96-06 and 96-07.
March 10, 1997	Letter to FDA (065) regarding KGL protocol, IRB approval, and consent form.
March 27, 1997	Letter to FDA (066) regarding revised protocol 96-LID-06 and 07.
March 28, 1997	Letter to FDA (067) regarding integrated clinical statistical report for 94-LID-05.
April 29, 1997	Letter to FDA (068) regarding final reports for 94-LID-01, 02 and 03.
August 2, 1997	Letter to FDA (069) regarding integrated clinical statistical report for 92-LID-03.
August 8, 1997	Letter to FDA (070) regarding integrated clinical statistical report for 95-LID-KS.
October 8, 1997	Letter to FDA (072) regarding pre-NDA meeting.
November 25, 1997	File NDA presubmission (075) drug substance, drug product and environmental assessment information, and nonclinical pharmacology, toxicology and pharmacokinetics.
December 22, 1997	Submit complete NDA (20-941).
December 22, 1998	Not-approvable letter received from FDA.
January 13, 1999	Letter to FDA requesting meeting to submit additional evidence of effectiveness.
February 26, 1999	Letter to FDA regarding Briefing Document for meeting to discuss non-approval letter.
March 1, 1999	Briefing Document sent to FDA in advance of meeting.

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March 18, 1999	Letter to FDA regarding response to request for amendment to NDA regarding chemistry, microbiology and pharmacology/toxicology comments.
March 24, 1999	Submit Amendment to NDA.
March 29, 1999	Submit Amendment to NDA regarding additional evidence of effectiveness.
April 30, 1999	Response to FDA questions regarding clinical study 92-LID-02.
May 5, 1999	Letter to FDA with statistical information requested by reviewing statistician.
May 14, 1999	Letter to FDA with completed TABLE A of Briefing Document and request for meeting on biostatistical issues.
May 24, 1999	Letter to FDA with request for expedited review by the Labeling and Nomenclature Committee and submission of revised product labeling.
June 8, 1999	Meeting with FDA statisticians to discuss additional evidence of effectiveness.
June 25, 1999	Letter to FDA regarding statistical issues.
August 3, 1999	Letter to FDA with response to question regarding suggested statistical analysis.
September 24, 1999	FDA informs AVANIR that available clinical data is insufficient to establish effectiveness.
September 30, 1999	Letter to CDER Ombudsman regarding chronology of events and AVANIR/FDA communications.
October 13, 1999	File formal dispute resolution request.
October 29, 1999	Teleconference with FDA indicating that 92-LID-02 will be sufficient as a second study to consider docosanol cream as an OTC.
November 22, 1999	FDA requests additional information.
December 2, 1999	File complete response to FDA request for additional information.
December 9, 1999	Audit of clinical study 92-LID-02 completed, form 483 issued.
January 21, 2000	Submitted form 483 response.
May 30, 2000	Approvable letter received from FDA, pending finalization of acceptable labeling.
June 6, 2000	Letter to FDA regarding various product OTC labels.
June 12, 2000	Letter to FDA regarding formal Dispute Resolution Request (regarding labeling).
July 25, 2000	Marketing approval letter received from FDA.

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Issued : October 17, 1989

- (12) *A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of extension claimed, including how the length of extension was determined.*

AVANIR Pharmaceuticals believes that it is entitled to an extension of term for U. S. Patent No. 4,874,794 (the Patent) in accordance with the provisions of 35 U.S.C. § 156. AVANIR Pharmaceuticals believes that the period of extension applicable to the patent is 5 years (1826 days), based on the following calculation in accordance with 37 C.F.R. § 1.775 (subsections listed below):

(c) The length of the regulatory review period for the approved product is calculated as the sum of:

(1) The number of days in the period beginning on the date of exemption under 35 U.S.C. §156(g)(1)(B)(i) from July 11, 1991 (the effective date of the IND) until December 22, 1997 (the NDA submission date) which is 2356 days; and

(2) The number of days in the review period under 35 U.S.C. §156(g)(1)(B)(i) from December 22, 1997 (the NDA submission date) until July 25, 2000 (marketing approval date), which is 946 days.

Thus, the total regulatory review period under 37 C.F.R. § 1.775(c) is 3302 days.

(d) The term is determined as follows:

(1) The sum of the following is subtracted from the regulatory review period (3302 days) as determined above:

(i) The number of days in the regulatory review period which were on or before the date on which the Patent issued. As the regulatory review commenced after the Patent issued, the number of days is 0 days.

(ii) The number of days in the regulatory review period wherein the Applicant did not act with due diligence, which is 0 days.

(iii) One-half the number of days remaining in the period defined by paragraph (c)(1) (2356 days) that has been reduced in accordance with the two items above, which is  $2356 \div 2 =$  1178 days.

Thus, the term under subsection (d) is  $3302 \text{ days} - 1178 \text{ days} =$  2124 days.

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Issued : October 17, 1989

(2) The date of expiration of the patent is extended by adding the number of days determined in (d)(1) (2124 days) to the original term of the patent, i.e., April 28, 2009 plus 2124 days, or February 20, 2015.

(3) Add 14-years to the date of approval (July 25, 2000), which would be July 25, 2014.

(4) Compare the dates of expiration obtained under paragraph (d)(2) and (d)(3) above and select the earlier date. Accordingly, July 25, 2014 is earlier than February 20, 2015.

(5) U.S. Patent No. 4,874,794 issued on October 17, 1989, which is after September 24, 1984. Accordingly, paragraph (5) is applicable.

(i) Add 5 years to the date of expiration of the patent (April 28, 2009), which would be April 28, 2014.

(ii) Compare the dates of expiration obtained under paragraphs (d)(4) and (d)(5)(i) above and select the earlier date. Accordingly, April 28, 2014 is earlier than July 25, 2014.

Thus, a 5-year extension from the original date of expiration is the maximum allowable extension available to AVANIR on U.S. Patent No. 4,874,794 under 37 C.F.R. §1.775.

**(13) *A statement that applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought (37 C.F.R. §1.765).***

AVANIR Pharmaceuticals acknowledges a duty to disclose to the Commissioner of Patents and Trademarks (and to the Patent and Trademark Office), and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought.

**(14) *The prescribed fee for receiving and acting upon the application for extension (37 C.F.R. § 1.20 (j)).***

AVANIR Pharmaceuticals hereby encloses a check in the amount of \$1,120.00, the prescribed fee under 37 C.F.R. § 1.20 (j). If for any reason this payment is insufficient, applicant

Patent No : U.S. 4,874,794  
Issued : October 17, 1989

hereby authorizes that any deficiency may be charged, or any overpayment credited, to Deposit Account No. 11-1410.

(15) *The name, address and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed.*

Please direct all correspondence relating to this application to:

Mark R. Benedict  
Registration No. 44,531  
Attorney of Record  
620 Newport Center Drive, Sixteenth Floor  
Newport Beach, CA 92660  
Telephone: (949) 760-0404  
Direct line: (949) 721-6323  
Facsimile: (949) 760-9502  
E-mail: mbenedict@kmob.com

(16) *A duplicate of the application papers, certified as such.*

AVANIR Pharmaceuticals hereby certifies that this application for patent term extension and supporting papers is being filed in duplicate, and certifies that the copy is a true copy of the original application and supporting papers.

(17) *An oath or declaration.*

A Declaration as set forth in 37 C.F.R. §1.740 (b) accompanies the present Application as Exhibit F.

If this application for extension of patent term is held to be informal, AVANIR Pharmaceuticals may seek to have the holding reviewed by filing a petition with the required fee, as necessary, pursuant to 37 C.F.R. § 1.181 or 1.183, as appropriate, within such time as may be set in any notice that the application has been held to be informal, or if no time is set, within one month of the date on which the application was held informal.

Patent No : U.S. 4,874,794  
Issued : October 17, 1989

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: \_\_\_\_\_

9/22/00

By: \_\_\_\_\_



Mark R. Benedict  
Registration No. 44,531  
Attorney of Record  
620 Newport Center Drive  
Sixteenth Floor  
Newport Beach, CA 92660  
(949) 760-0404

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of :	KATZ, David H.	)	Group Art Unit 125
		)	
Appl. No. :	07/345,084	)	
Filed :	April 28, 1989	)	
		)	
Patent No. :	U. S. Patent No. 4,874,794	)	
		)	
Issued :	October 17, 1989	)	
		)	
For :	INFLAMMATORY DISEASE TREATMENT	)	
		)	
Examiner :	FRIEDMAN, Stanley J.	)	
		)	
		)	

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OFFICE OF PETITIONS

Assistant Commissioner for Patents  
Washington, D.C. 20231  
Box Patent Ext.

DECLARATION UNDER 37 C.F.R. §1.740(b) FOR EXTENSION OF PATENT TERM

I Mark R. Benedict, patent attorney with the firm of Knobbe, Martens, Olson & Bear, LLP, and registered to practice before the Patent and Trademark Office, have Power of Attorney to act on behalf of the assignee, AVANIR Pharmaceuticals, the owner of the entire right, title and interest in U. S. Patent No. 4,874,794, in executing this Declaration and the attached application for extension of patent term.

I hereby declare the following:


- (1) I have reviewed and understand the contents of the application being submitted pursuant to 37 C.F.R. §1.740;
- (2) I believe the patent is subject to extension pursuant to §1.710;
- (3) I believe an extension of the length claimed is justified under 35 U.S.C. §156 and the applicable regulations; and
- (4) I believe the patent for which extension is sought meets the conditions for extension of the term of a patent as set forth in §1.720.



In re Patent of KATZ, David H.  
Declaration under 37 C.F.R. §1.740  
Page 2

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 9/22/00

  
Mark R. Benedict  
Registration No. 44,531  
Attorney of Record

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UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
Washington, D.C. 20231  
www.uspto.gov

NOV 27 2000

David T. Read  
Acting Director Regulatory Policy Staff, CDER  
Food and Drug Administration  
1451 Rockville Pike, HFD-7  
Rockville, MD 20852

Dear Mr. Read:

The attached application for patent term extension of U.S. Patent No. 4,874,794, was filed on September 25, 2000, under 35 U.S.C. § 156.

The assistance of your Office is requested in confirming that the product identified in the application, ABREVA™ (docosanol), has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within sixty days after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156.

Karin Tyson  
Senior Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner for Patent Examination Policy

cc: Mark R. Benedict  
620 Newport Center Drive, Sixteenth Floor  
Newport Beach CA 92660



MAR 14 2003

Mark R. Benedict  
Knobbe Martens Olsen & Bear, LLP  
620 Newport Center Drive, 16th Floor  
Newport Beach, CA 92660

Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,874,794

## NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,874,794, which claims the human drug product ABREVA™ (docosanol), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 5 years.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Director will issue a certificate of extension, under seal, for a period of 5 years.

The period of extension has been calculated using the Food and Drug Administration determination of the length of the regulatory review period published in the Federal Register of February 28, 2002 (67 Fed. Reg. 9303). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (2,323) + 947 \\ &= 2,109 \text{ days (5.8 years)}\end{aligned}$$

Since the regulatory review period began August 14, 1991, after the patent issue date (October 17, 1989), the entire period has been considered in the above determination. No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The five year limitation of 35 U.S.C. § 156(g)(6)(A) applies in the present situation, however, because the patent was issued after the date of enactment (September 24, 1984) of 35 U.S.C. § 156. Since the period of extension calculated under 35 U.S.C. § 156(c) for the patent cannot exceed five years under 35 U.S.C. § 156(g)(6)(A), the period of extension will be for five years.

The 14 year limitation of 35 U.S.C. § 156(c)(3) does not operate to further reduce the period of extension determined above.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.:	4,874,794
Granted:	October 17, 1989
Original Expiration Date <sup>1</sup> :	April 28, 2009

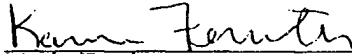
<sup>1</sup>Subject to payment of any required maintenance fees.

Applicant: David H. Katz  
Owner of Record: AVANIR Pharmaceuticals  
Title: Inflammatory Disease Treatment  
Classification: 514/724  
Product Trade Name: ABREVA™ (docosanol)  
Term Extended: 5 years  
Expiration Date of Extension: April 28, 2014

Any correspondence with respect to this matter should be addressed as follows:

By mail: Commissioner for Patents      By FAX: (703) 872-9411  
Box Patent Ext.      Attn: Office of Patent Legal Administration  
Washington, D.C. 20231

Telephone inquiries related to this determination should be directed to the undersigned at  
(703) 306-3159.

  
Karin Ferriter  
Senior Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

cc: David T. Read  
Acting Director Health Assessment Policy Staff, CDER  
Food and Drug Administration  
1451 Rockville Pike, HFD-7  
Rockville, MD 20852

RE: ABREVA™ (docosanol)  
FDA Docket No.: 01E-0090



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#30

the Patent of:

Marshall et al.

Patent No. 4,941,093

Issued: July 10, 1990

Title: SURFACE EROSION USING LASERS

EXPRESS MAILING CERTIFICATE

Express Mailing Label No. TB281196520 US  
Date of Deposit: May 9, 1995

I hereby certify that this document is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Assistant Commissioner for Patents, Box Patent Extension, Washington, D.C. 20231.

Viriato G. Cardoso  
Viriato G. Cardoso

APPLICATION FOR EXTENSION OF PATENT TERM  
UNDER 35 U.S.C. §156

Assistant Commissioner for Patents  
Box Patent Extension  
Washington, DC 20231

Dear Sir:

Pursuant to the provisions of 35 U.S.C. §156, and in compliance with 37 C.F.R. §§1.710 *et seq.*, Summit Technology, Inc., a corporation of Massachusetts having its principal place of business located at 21 Hickory Drive, Waltham, Massachusetts 02154, and the owner of record of the above-cited patent, by its undersigned agent, hereby makes application for an extension of the patent term of its United States Patent No. 4,941,093.

(1) The approved products that are the subject of this application are medical devices known as the Excimer® UV200LA and the SVS Apex (formerly the OmniMed) Excimer Laser Systems which presently are indicated for use in the certain Phototherapeutic Keratectomy (PTK) procedures for treatment of superficial pathologies of the cornea. Additional approved uses are also anticipated. The approved products are laser systems which precisely erode (ablate) corneal tissue in a manner that reduces or alleviates the corneal irregularities causing such pathologies. The approved products are systems which include, *inter alia*, a source of laser radiation that is at an energy level sufficient to induce photoablation of biological tissue, support and/or alignment means for directing the laser radiation onto a target tissue surface, e.g., the corneal surface of an eye, and a beam dimension control mechanism which permits the user to vary the area on the target surface exposed to the laser radiation while maintaining a substantially constant energy per unit area during each pulse.

(2) The regulatory review of the approved product was conducted by the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) under Sections 515 and 520 of the Federal Food, Drug, and Cosmetic Act. The approved products are presently approved for use on patients having decreased visual acuity or symptoms of pain and discomfort of sufficient severity to cause disability (i.e., superficial corneal dystrophies, epithelial basement membrane dystrophy, irregular corneal surfaces, and corneal scars and opacities). It is anticipated that additional uses for the approved products, such as Photorefractive Keratectomy (PRK) in which the curvature of the cornea is modified to correct refractive errors in vision, will be authorized by the FDA in the future.

(3) By letter dated March 10, 1995, the Office of Device Evaluation of the Center for Devices and Radiological Health approved commercial sale, distribution and use of the approved product subject to compliance with certain post-approval requirements.

(4) This Application is being submitted within the sixty-day (60) period permitted for submission of such applications for extension of patent terms pursuant to 37 C.F.R. §1.720(f), the last day of said sixty-day (60) period being May 9, 1995.

(5) United States Patent No. 4,941,093 for a "Surface Erosion Using Lasers" is the patent for which a term extension is being sought. United States Patent No. 4,941,093 issued on July 10, 1990, naming as inventors John Marshall, Anthony L. Raven, Walter T. Welford, and Karen M. M. Ness with Summit Technology, Inc., as Assignee, and expiring on July 10, 2007.

(6) A copy of United States Patent No. 4,941,093, including the entire specification (including claims) and drawings, is attached hereto as **Exhibit A**.

(7) Attached as **Exhibit B** hereto are copies of the Certificates of Correction, which were issued by the Commissioner of Patents on December 31, 1991 and July 28, 1992, with respect to U.S. Patent No. 4,941,093. Attached as **Exhibit C** hereto is a copy of a Maintenance Fee Statement receipt dated December 21, 1993, relating to United States Patent No. 4,941,093. There are no other disclaimers, certificates of correction, receipts of maintenance fee payments, or re-examination certificates that have issued to date in United States Patent No. 4,941,093.

(8) Claims 1-10, 12, 15-18, 21-23, 25, 27-32 and 35-37 of United States Patent No. 4,941,093 read on the approved products identified in paragraph (1) above. The identified claims are believed to encompass both PTK procedures, which typically involve a smaller (and/or shallower) corneal ablation zone, and PRK procedures, which typically involve ablation of larger regions of the cornea. The following is a showing which lists each applicable claim of said patent and demonstrates the manner in which it reads on the approved products (or method of using the same):



*1. A laser system for eroding a surface, said laser system comprising:*

*laser means for generating pulses of laser light along a beam path at an energy level, such that the pulses can be absorbed at a surface to induce photoablation;*  
*support means for aligning a surface relative to the laser means; and*  
*beam dimension control means disposed along said laser beam path, including optical means for optically varying an area on the surface to which the pulses of laser energy are delivered while maintaining a substantially constant energy per unit area during each pulse.*

The approved products are laser systems for eroding the surface of the cornea. The approved products include a laser, support structures and a beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

*2. A laser system according to claim 1 and further comprising optical beam-shaping means for varying the shape of the area of the surface to which the pulses are delivered.*

The approved product is an surgical excimer laser system that includes means for varying the shape of the exposure area of the surface to which pulses of radiation are delivered.

*3. A laser system according to claim 1 in which the laser means generates from about 1 to about 500 pulses per second.*

The approved product is an surgical excimer laser system that includes means for generating pulses of radiation within the range of about 1 to about 500 pulses per second.

*4. A laser system according to claim 1 in which said control means further comprises beam-shaping means for receiving a laser beam provided by said laser means and for shaping the beam by passage through an aperture, the beam-shaping means being disposed about an optical axis of the laser beam, such that movement along the optical axis varies the cross-sectional area of the beam which passes through the aperture.*

The approved product is an surgical excimer laser system that includes a beam-shaping aperture which is movable along an optical axis to vary the cross-sectional area of the beam.

5. *A laser system according to claim 4 which further comprises a focusing means for focusing an image of the aperture of the beam-shaping means onto the surface to be eroded.*

The approved product is an surgical excimer laser system that includes an imaging means that relays an image of an aperture onto the target surface.

6. *A method of eroding a surface by laser energy, said method comprising the steps of:  
aligning a surface with a laser means, which is operable to deliver a beam of photoablative pulses of laser energy along a path to the surface;  
adjusting the size of the area on the surface to which the pulses are delivered; and  
operating a beam dimension control means disposed along said path for optically controlling said beam to deliver pulses of laser energy of variable cross-sectional area to the surface while maintaining a substantially constant energy per unit area during each pulse.*

The approved product is an surgical excimer laser system that can be used in a manner in which the area of the beam is adjusted to deliver pulses of laser energy of variable cross-sectional area to the surface while maintaining a substantially constant energy per unit area during each pulse.

7. *A method according to claim 6 in which the shape of the area on the surface to which the pulses are delivered is adjusted in a controlled manner thereby selecting the shape of the area eroded by the pulses.*

The approved product can likewise be used in a manner in which the shape of the exposure area is adjusted.

8. *A method according to claim 6 in which the size of the area to be eroded by said pulses is varied in a controlled manner during said step of operating the laser.*

The approved product can likewise be used in a manner in which the size of the exposure area is varied during operation of the laser.

9. *A method according to claim 6 in which following said step of adjusting the size of the area to be eroded, the size of said area to be eroded is maintained substantially constant during said step of operating the laser.*

The approved product can also be used in a manner in which the size of the exposure area is maintained substantially constant during operation of the laser.

10. *A laser system for eroding and thereby shaping or reprofiling a surface, said laser system comprising:*

*support means for aligning a surface to be eroded relative to an optical axis (or vice versa),*

*a beam delivery system for relaying energy from a laser light source onto the surface along said optical axis,*

*a laser light source, power supply and an associated control circuit for generating pulses of laser energy for application to the surface; and*

*beam dimension control means disposed along said optical axis, including optical means for optically controlling the area over which the pulses of laser energy are applied to the surface while maintaining a substantially constant energy per unit area during each pulse, thereby causing greater or lesser ablation of selected regions of the surface.*

The approved products are laser systems for eroding the surface of the cornea. The approved products include a laser, optical delivery assemblies, support structures and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

12. *A laser system according to claim 10 in which the energy density of the laser pulses applied to the surface is above the threshold value for ablation of corneal tissue and not substantially higher than the saturation level for ablation of corneal tissue.*

The approved products can be calibrated (and typically are calibrated) such that the energy density of the laser pulses applied to the surface is above the threshold value for ablation of corneal tissue and not substantially higher than the saturation level for ablation of corneal tissue.

15. *A method of eroding a surface of an object, said method comprising the steps of:*

*aligning a surface of an object with a laser source which is operable to deliver pulses of laser energy to the surface,*

*pulsing the laser source along a path so that light therefrom falls on the surface of the object, and*

*controlling the light from the laser with a beam dimension control means disposed along said path so as to optically vary the area over which the light is incident during the emission of a plurality of pulses, thereby selectively exposing areas of the surface to a greater or lesser extent while maintaining a substantially constant energy per unit area during each pulse, and thereby obtaining a desired erosion profile of the surface.*

The approved products are laser systems for eroding the surface of the cornea. The approved products include a pulsed source of laser radiation, alignment means, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

*16. A method according to claim 15 in which the laser wavelength is selected so that the laser energy incident on the surface of the object is absorbed by the material forming the surface, so that there is little or no energy remaining to penetrate and affect the material below the surface.*

The wavelength employed by the approved product is about 193 nanometers; this ultraviolet radiation is absorbed by only the uppermost layers of the corneal surface such that there is little or no energy remaining to penetrate and affect the material below the surface.

*17. A method according to claim 15 in which pulses of energy are directed towards selected overlapping regions of the surface, so that, over a period of time, different regions of the surface are exposed to different quantities of energy from the laser source, so as to produce differential erosion of the surface.*

During the course of using the approved products, the clinician can direct pulses of radiation towards selected overlapping regions of the surface, so that, over a period of time, different regions of the surface are exposed to different quantities of energy from the laser source, so as to produce differential erosion of the surface.

*18. A method according to claim 15 in which the energy density of the laser pulses falling on the surface is greater than the threshold for ablation but not substantially greater than the saturation level for ablation of the material of the object.*

The approved products can be calibrated (and typically are calibrated) such that the energy density of the laser pulses applied to the surface is above the threshold value for ablation of corneal tissue and not substantially higher than the saturation level for ablation of corneal tissue.

21. *A method of eroding an area of a cornea of an eye said method comprising the steps of:*  
*fixing an eye relative to laser means operable to deliver a beam of photoablative pulses*  
*of laser energy along a path to the surface of the cornea;*  
*varying the area on the surface of the cornea to which the pulses are delivered in a*  
*controlled manner; and*  
*operating a beam dimension control means disposed along said path for optically*  
*controlling said beam to deliver pulses of laser to the varied areas of the surface while*  
*maintaining a substantially constant energy per unit area during each pulse.*

The approved products are laser systems for eroding the surface of the cornea. The approved products include a source of pulsed laser radiation, means for directing such radiation onto the corneal surface of an eye, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

22. *A method of removing corneal ulcers comprising steps of:*  
*fixing an eye relative to laser means operable to deliver a beam of photoablative pulses*  
*of laser energy along a path to the surface of the cornea;*  
*varying the area on the surface of the cornea to which the pulses are delivered in a*  
*controlled manner so as to expose the corneal ulcer; and*  
*operating a beam dimension control means disposed along said path for optically*  
*controlling said beam to deliver pulses of laser energy of variable cross-sectional area to the*  
*ulcer while maintaining a substantially constant energy per unit area during each pulse.*

The approved products are laser system for eroding the surface of the cornea. The approved products include a source of pulsed laser radiation, means for directing such radiation onto the corneal surface of an eye, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

23. *A method of preparing a bed for a corneal transplant in which corneal material is removed*  
*by erosion using a method comprising the steps of:*  
*fixing an eye relative to the laser means to deliver a beam of photoablative pulses of laser*  
*energy along a path to the surface of the cornea;*  
*varying the area on the surface of the cornea to which the pulses are delivered in a*  
*controlled manner so as to expose a corneal transplant bed; and*  
*operating a beam dimension control means disposed along said path for optically*  
*controlling said beam to deliver pulses of laser energy of variable cross-sectional area to the*  
*transplant bed while maintaining a substantially constant energy per unit area during each*  
*pulse.*

The approved products are laser system for eroding the surface of the cornea. The approved products include a source of pulsed laser radiation, means for directing such radiation onto the corneal surface of an eye, which can be a corneal transplant bed, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

*25. A method of correcting ocular disorders by reprofiling a corneal surface of an eye, the method comprising the steps of:*

*aligning a cornea of an eye with a laser which, in use, generates a beam of laser light capable of photoablating corneal tissue;*

*pulsing the laser source so that light therefrom propagates along a path and falls intermittently on the surface of the cornea to induce photoablation of a thin surface layer of the cornea within an area of exposure during each pulse;*

*controlling the light with a beam dimension control means disposed along said path from the laser to optically vary said area of exposure while maintaining a substantially constant energy per unit area during each pulse, whereby a reprofiled corneal surface is obtained as a result of variations in the total energy delivered to selected regions of corneal surface.*

The approved products are laser systems for reprofiling the surface of the cornea. The approved products include a pulsed source of laser radiation, means for aligning the cornea with the laser, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

*27. The method of claim 25 wherein the step of pulsing the laser source to induce photoablation further comprises delivering ultraviolet light to the surface of the cornea.*

The approved product employs an Argon-Fluoride (ArF) excimer laser generating ultraviolet radiation at a wavelength of about 193 nanometers.

*28. The method of claim 27 wherein the step of delivering ultraviolet light to the surface of the cornea further comprises delivering ultraviolet light at a wavelength of about 193 nanometers.*

Again, the approved product employs an Argon-Fluoride (ArF) excimer laser generating ultraviolet radiation at a wavelength of about 193 nanometers.

29. *The method of claim 25 wherein the step of pulsing the laser source to induce photoablation of the cornea further comprises delivering laser light at an energy level ranging from about 0.1 to about 1.0 Joules/cm<sup>2</sup>.*

The approved product is an surgical excimer laser system that includes means for generating pulses of radiation at an energy level within the range of about 0.1 to about 1.0 Joules/cm<sup>2</sup>.

30. *The method of claim 25 wherein the step of controlling the light from the laser further comprises varying the area of exposure to obtain a general flattening of the surface of the cornea and thereby decrease the refractive power of the eye.*

The approved products are laser systems for reprofiling the surface of the cornea. The approved products include a pulsed source of laser radiation, means for aligning the cornea with the laser, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area. In use, such products can effect a general flattening of the cornea.

31. *The method of claim 25 wherein the step of controlling the light from the laser further comprises varying the area of exposure to increase the curvature of the cornea and thereby increase the refractive power of the eye.*

The approved products are laser systems for reprofiling the surface of the cornea. The approved products include a pulsed source of laser radiation, means for aligning the cornea with the laser, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area. In use, the approved products can, likewise, increase the corneal curvature.

32. *The method of claim 25 wherein the step of controlling the light from the laser further comprises varying a non-circular area of exposure to correct astigmatisms.*

The approved products are laser systems for reprofiling the surface of the cornea. The approved products include a pulsed source of laser radiation, means for aligning the cornea with the laser, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area. In use the approved products can also expose non-circular areas of the cornea.

35. *A corneal reprofiling system for modifying the surface of a cornea of an eye, the system comprising:*

*a laser means generating a beam of pulses of laser light along a path at an energy level, such that the light pulses can be absorbed in a thin surface layer of a cornea of an eye to induce photoablation;*

*a support means for aligning an eye relative to the laser means; and*

*a beam dimension control means disposed along the path, including a beam-forming optical means for optically varying a area over which the laser light is incident while maintaining a substantially constant energy per unit area during each pulse.*

The approved products are laser systems for modifying the surface of the cornea. The approved products include a pulsed source of laser radiation, support means for aligning the cornea with the laser, and beam control means which can vary the area of exposure while maintaining a substantially constant energy density per unit area.

36. *The system of claim 35 wherein the laser means generates pulses of ultraviolet laser light at a wavelength of about 193 nanometers.*

The approved product employs an Argon-Fluoride (ArF) excimer laser generating ultraviolet radiation at a wavelength of about 193 nanometers.

37. *The system of claim 36 wherein the laser means generates pulses of laser light at an energy level ranging from about 0.1 to about 1.0 Joules/cm<sup>2</sup> (as corrected by Certificate of Correction dated December 31, 1991).*

The approved product is an surgical excimer laser system that includes means for generating pulses of radiation at an energy level within the range of about 0.1 to about 1.0 Joules/cm<sup>2</sup>.



(9) The relevant dates and information pertinent to 35 U.S.C. §156(g) and 37 C.F.R. §1.740(a)(10)(v), are provided in order to enable the Secretary of Health and Human Services to determine the applicable regulatory review period:

12-22-88	The effective date of investigation device exemption (IDE) #G880234. On this date, a letter of approval was issued conditional on compliance with certain formalities.
09-09-89	The date on which a clinical investigation on humans was begun.
11-19-91	The date on which an application for product approval was initially submitted under PMA #P910067.
03-10-95	The date PMA #P910067 was approved.

(10) A brief description of the activities undertaken during the applicable "regulatory review period" with respect to the approved product, and the significant dates applicable to such activities, follow:

**IDE Clinical Trial Program**

- |  |                    |
|--|--------------------|
| • IDE Submitted                              | September 28, 1988 |
| Conditional Approval                         | December 22, 1988  |
| Full Approval Phase I                        | February 3, 1989   |
| • Clinical Investigation on Humans Begun     | September 9, 1989  |
| • Phase I Progress Report                    | March 9, 1990      |
| Approval to Phase II                         | April 11, 1990     |
| • Phase II Progress Report                   | November 1, 1990   |
| Conditional Approval for additional patients | February 15, 1991  |
| • PMA for PTK Submitted                      | November 19, 1991  |

**Ongoing IDE Clinical Trial Activities**

- |                        |                               |
|------------------------|-------------------------------|
| • Phase II - Extension | December 12, 1991 - Submitted |
|                        | January 15, 1992 - Approved   |
| • Phase III            | January 13, 1993 - Submitted  |
|                        | February 12, 1993 - Approved  |

**PMA Approval Process**

- |   |                            |
|---|----------------------------|
| • Submission of PMA Application   | November 19, 1991          |
| • Amendment 1<br>Response to FDA questions  | February 2, 1992           |
| • Amendment 2<br>Response to FDA letter of 2/7/92   | February 19, 1992          |
| • PMA Filed by FDA  | February 20, 1992          |
| • FDA GMP Inspection Waltham  | February 24, 25 & 27, 1992 |
| • FDA GMP Inspection Cork   | April 3-4, 1992            |
| • Amendment 3<br>Safety and Effectiveness filing  | May 19, 1992               |
| • Amendment 4<br>Documentation to add additional<br>products to PMA                                   | October 23, 1992           |
| • Amendment 5<br>To grant FDA permission to access safety<br>and efficacy data in related submissions | December 15, 1993          |
| • Amendment 6<br>Response to further FDA questions  | December 20, 1993          |
| • Amendment 7<br>Pre-panel clinical update and<br>comprehensive summary                               | January 17, 1994           |
| • Amendment 8<br>Submission of additional data  | January 28, 1994           |

- Amendment 9  
Submission of materials for primary reviewers. February 4, 1994
- Amendment 10  
Additional copies of materials for PMA reviewers February 24, 1994
- Ophthalmic Advisory Panel  
Review March 21, 1994  
Panel Granted Conditional Approval
- Amendment 11  
Response to FDA questions March 28, 1994
- Amendment 12  
Submission of answers to questions from panel meeting March 31, 1994
- FDA Approvable Letter Received June 14, 1994
- Amendment 13  
Submission of updated Safety and Effectiveness information in accord with "Conditions of Approval" July 18, 1994
- Amendment 14  
Submission of further statistical analysis of data January 12, 1995
- Amendment 15  
Submission of further product description December 19, 1994
- Amendment 16  
Submission of further reports December 20, 1994
- Amendment 17  
Submission of updated User's Manual January 13, 1995
- Amendment 18  
Notify FDA of name change - Apex. January 23, 1995
- Amendment 19  
Submission of further User's Manual changes January 15, 1995

- Amendment 20  
Submission of further User's  
Manual changes January 27, 1995
- Amendment 21  
Submission of further User's  
Manual changes January 30, 1995
- Amendment 22  
Submit final labeling to FDA and  
Final Physician Guidelines March 8, 1995
- **COMMERCIAL APPROVAL** March 10, 1995

(11) In the opinion of the Applicant, Summit Technology, Inc., United States Patent No. 4,941,093 is eligible for an extension of 609 days from July 10, 2007 (the original expiration date), to and including March 10, 2009 is being requested hereby. A worksheet showing how the length of the extension was determined is attached hereto. Although the period of extension, calculated pursuant to 37 CFR 1.777(d)(2), amounts to 1455 days, the exception of 35 USC 156(c)(3) appears to apply and operates to limit the term of extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the product (March 10, 1995) when added to the calculated period of extension can not exceed 14 years. The period of extension is thus limited to March 10, 2009 (609 days) by operation of 35 USC 156(c)(3).

(12) Summit Technology, Inc., acknowledges its duty to disclose to the Assistant Commissioner for Patents and to the Secretary of Health and Human Services any information that is material to the determination of entitlement to the extension sought.

(13) The prescribed fee of \$1,030.00 for receiving and acting upon the instant application for extension of patent term is submitted herewith.


(14) The name, address, and telephone number of the person to whom inquiries and correspondence relating to this application are to be directed is: Thomas J. Engellenner, Esq., Lahive & Cockfield, 60 State Street, Boston, Massachusetts 02109, (617) 227-7400.

(15) Four duplicates of these application papers, certified as such, are submitted herewith.

(16) A declaration as set forth in 37 C.F.R. 1.740(a)(17) is also submitted herewith.

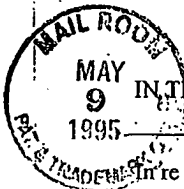
Respectfully Submitted,

LAHIVE & COCKFIELD

  
Thomas J. Engellenner  
Attorney for Patentee  
Registration No. 28,711

Dated: May 9, 1995

60 State Street  
Boston, Massachusetts 02109  
Tel.: (617) 227-7400



111-1030.00  
A/C for Patents

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent of:

Marshall et al.

Patent No. 4,941,093

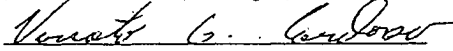
Issued: July 10, 1990

Title: SURFACE EROSION USING LASERS

EXPRESS MAILING CERTIFICATE

Express Mailing Label No. TB281196520 US  
Date of Deposit: May 9, 1995

I hereby certify that this document is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Assistant Commissioner for Patents, Box Patent Extension, Washington, D.C. 20231.

  
Viriato G. Cardoso

DECLARATION

Assistant Commissioner for Patents  
Box Patent Extension  
Washington, DC 20231

Dear Sir:

I Thomas J. Engellenner, residing at 11 Birch Hill Road, Newton, Massachusetts 02165  
declare and state as follows:

(1) That I am a patent attorney authorized to practice before the Patent and Trademark Office and I have general authority from Summit Technology, Inc., owner of U.S. Patent No. 4,941,093, to act on its behalf in connection with its application for patent term extension of U.S. Patent No. 4,941,093;

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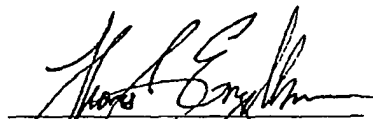
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- (2) I have reviewed and understand the contents of the application for Extension of Patent Term being submitted herewith pursuant to 35 U.S.C 156 and 37 C.F.R. 1.710 *et seq*;
- (3) I believe the patent is subject to extension pursuant to 35 U.S.C 156 and 37 C.F.R. 1.710;
- (4) I believe an extension of the length claimed in the accompanying application is justified under 35 U.S.C. 156 and the applicable regulations; and
- (5) I believe that the patent for which extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. 1.710.

I hereby declare that all statements made herein of my own knowledge are believed true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the accompanying application and any extension of U.S. Patent No. 4,941,093.

May 9, 1995  
Date

  
Thomas J. Engellennet, Esq.  
Reg. No. 28,711



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent of:

Marshall et al.

Patent No. 4,941,093

Issued: July 10, 1990

Title: SURFACE EROSION USING LASERS

EXPRESS MAILING CERTIFICATE

Express Mailing Label No. TB281196520 US  
Date of Deposit: May 9, 1995

I hereby certify that these materials are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Assistant Commissioner for Patents, Box Patent Extension, Washington, D.C. 20231.

*Viriato G. Cardoso*  
Viriato G. Cardoso

TRANSMITTAL LETTER

Assistant Commissioner for Patents  
Box Patent Extension  
Washington, DC 20231

Dear Sir:

Transmitted herewith are five copies of the application for Extension of Patent Term under 35 U.S.C. 156 with regard to U.S. Patent No. 4,941,093, together with Attachment 1, Exhibits A-C, and Declaration.

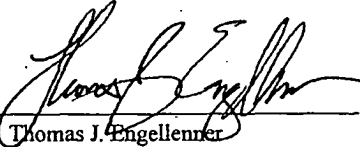
A check for \$1,030.00 is also enclosed. Please charge any additional fees which

may be required, or, credit any overpayments to Deposit Account No. 12-0080. A  
duplicate copy of this paper is enclosed.

Respectfully submitted,

LAHIVE & COCKFIELD

By



Thomas J. Engellenner  
Registration No. 28,711

60 State Street  
Boston, MA 02109  
Telephone Number: (617) 227-7400  
May 9, 1995



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

MAY 19 1995

#31

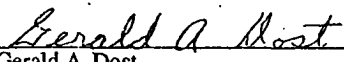
Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fisher's Lane, Room 11-44  
Rockville, MD 20857

Dear Mr. Wilson:

The enclosed application for extension of the patent term of U.S. Patent No. 4,941,093 issued on July 10, 1990, was filed on May 9, 1995, under 35 U.S.C. 156.

Your assistance is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 USC § 156(g) before its commercial marketing or use. Since a determination has not been made whether the patent in question claims a product which is subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. 156(d)(2)(A).

Our review of the application to date indicates that the subject matter would be eligible for extension of the patent term under 35 U.S.C. 156.

  
Gerald A. Dost  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

(703) 305-9285

cc: Thomas J. Engellenner  
Lahive & Cockfield  
60 State Street  
Boston, MA 02109



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

JUN 21 1995

Re: Excimed UV200LA / SVS APEX Excimer  
Laser Systems  
Docket No. 95E-0147

#32

Stephen G. Kunin  
Deputy Assistant Commissioner for  
Patent Policy and Projects  
Office of the Assistant Commissioner for Patents  
U.S. Patent and Trademark Office  
Crystal Park Building 2, Suite 919  
Washington, D.C. 20231

RECEIVED  
JUN 23 1995  
OFFICE OF THE ASSISTANT  
COMMISSIONER FOR PATENTS

Dear Mr. Kunin:

This is in regard to the application for patent term extension for U.S. Patent No. 4,941,093 filed by Summitt Technology, Inc., under 35 U.S.C. § 156. The medical device claimed by the patent is Excimed UV200LA / SVS APEX Excimer Laser Systems.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of this product under section 515(d) of the Federal Food, Drug, and Cosmetic Act.

The PMA was approved on March 10, 1995, which makes the submission of the patent term extension application on May 9, 1995, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Thomas J. Engellenner  
Lahive & Cockfield  
60 State Street  
Boston, MA 02109

1996 10 10



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

#87

Thomas J. Engellener, Esq.  
Lahive & Cockfield  
60 State Street  
Boston, MA 02109

Re: Patent Term Extension  
Application for  
U.S. Patent No. 4,941,093

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 4,941,093, which issued July 10, 1990 and which claims the medical device Excimid® UV200LA/SVS Apex (Excimer Laser Systems), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 609 days.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of August 7, 1995 (60 Fed. Reg. 40,183). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= 1/2 \text{ (Testing Phase) } + \text{ Approval Phase} \\ &= 1/2 (1,156 - 565) + 1,115 \\ &= 1,411 \text{ days}\end{aligned}$$

Since the regulatory review period began December 22, 1988, before the patent issued (July 10, 1990), only that portion of the regulatory review period occurring after the date the patent issued has been considered in the above determination of the length of the extension period 35 U.S.C. § 156(c). (From December 22, 1988 to July 10, 1990 is 565 days; this period is subtracted for the number of days occurring in the testing phase according to the FDA determination of the length of the regulatory review period:  $1,156 - 565 = 591$  days.) No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The 14 year exception of 35 U.S.C. § 156(c)(3) operates to limit the term of the extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the approved product (March 10, 1995) when added to the period of extension calculated above (1,380 days) cannot exceed fourteen years. The period of extension is thus limited to March 10, 2009, by operation of 35 U.S.C. § 156(c)(3).

Since the patent term of seventeen years (35 U.S.C. § 154)<sup>1</sup> would expire on July 7, 2007, the period of extension is the number of days to extend the term of the patent from its expiration date to and including March 10, 2009, or 609 days.

The limitations of 35 U.S.C. § 156(g)(6) do not operate to further reduce the period of extension determined above.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Commissioner will issue a certificate of extension, under seal, for a period of 609 days.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.:	4,941,093
Granted:	July 10, 1990
Applicant:	John Marshall et al.
Owner of Record:	Summit Technology, Inc.
Title:	SURFACE EROSION USING LASERS
Classification:	364/413.01
Product Trade Name:	Excimid® UV200LA/SVS Apex

<sup>1</sup> 35 U.S.C. § 154 was amended by the Uruguay Round Agreements Act to provide, in subsection (c)(1) thereof, that a patent in force on June 8, 1995 shall have the longer term of seventeen years from the issue date or 20 years from the filing date of the application or an earlier filed application to which a specific reference is made under 35 U.S.C. § 120, 121 or 365(c). The application that resulted in U.S. Patent No. 4,941,093 was a continuation-in-part of an application that was filed on June 2, 1986. Thus, the application contained a specific reference to an earlier application under 35 U.S.C. § 120 and 20 years from that date would have been, June 2, 2006, which is before July 10, 2007, the expiration of the seventeen year term. Since the original seventeen year term is longer than the new term defined by the amendment to § 154, it is unnecessary to determine whether the patent term extension can be added to the new term.

U.S. Patent No. 4,941,093

Page 3

(Excimer Laser Systems)

Term Extended: 609 days

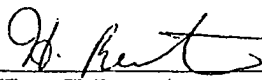
Any correspondence with respect to this matter from the applicant should be addressed as follows:

By mail: Assistant Commissioner for Patents  
Box DAC  
Washington, D.C. 20231

By FAX: (703) 308-6916  
Attn: Special Program Law Office

By hand: One Crystal Park, Suite 520  
2011 Crystal Drive  
Arlington, VA

Telephone inquiries should be directed to Karin Tyson at (703) 305-9285.

  
Hiram H. Bernstein  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

(703) 305-9285

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HPY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 11-44  
Rockville, MD 20857

RE: Excimid® UV200LA/SVS  
Apex (Excimer Laser Systems)  
FDA Docket No.: 95E-0147



UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

PATENT NO. : 4,941,093  
ISSUED : July 10, 1990  
INVENTOR(S) : John Marshall et al.  
PATENT OWNER : Summit Technology, Inc.

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

609 days

from the original expiration date of the patent, July 10, 2007, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 31st day of May 1996.

*Bruce A. Lehman*

Bruce A. Lehman  
Assistant Secretary of Commerce and  
Commissioner of Patents and Trademarks

BEST COPY

111-1000

PATENT  
Atty. Docket No.: 3036.0006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 5,441,745 )  
)  
Issued: August 15, 1995 )  
)  
To: Cary A. Presant, Richard T. Proffitt, )  
Raymond L. Teplitz, Lawrence E. )  
Williams, and George W. Tin )  
)  
Assignee: NeXstar Pharmaceuticals, Inc. )  
)  
For: METHOD OF DELIVERING )  
MICELLULAR PARTICLES ENCAP- )  
SULATING CHEMOTHERAPEUTIC )  
AGENTS TO TUMORS IN A BODY )

RECEIVED

JUN 7 1996

OFFICE OF PATENT  
AND TRADEMARKS

ATTN: BOX PATENT EXT.  
Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**APPLICATION FOR EXTENSION OF PATENT  
TERM UNDER 35 U.S.C. § 156**

Your Applicant, NeXstar Pharmaceuticals, Inc., represents that it is the Assignee of the entire interest in and to Letters Patent of the United States 5,441,745 granted to Cary A. Presant, Richard T. Proffitt, Raymond L. Teplitz, Lawrence E. Williams, and George W. Tin on the 15th day of August, 1995, for METHOD OF DELIVERING MICELLULAR PARTICLES ENCAPSULATING CHEMOTHERAPEUTIC AGENTS TO TUMORS IN A BODY by virtue of an assignment in favor of NeXstar Pharmaceuticals, Inc. The assignment to Vestar, Inc. was recorded at Reel 5614, Frame 0408, and Reel 4711, Frame 0249, and the merger into NeXstar Pharmaceuticals, Inc. was submitted for recordation to the U.S. Patent and Trademark

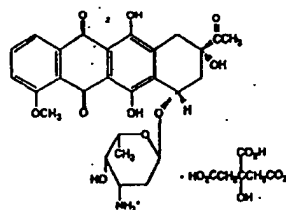
LAW OFFICES  
FINNEGAN, HENDERSON,  
FARABOW, GARRETT  
& DUNN, L.L.P.  
1300 I STREET, N.W.  
WASHINGTON, DC 20005  
202-408-4000

Office on March 1, 1996. A copy of the documents submitted for recordation is attached as Attachment A. By the Power of Attorney enclosed herein (Attachment B), Applicant appoints Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., including Charles E. Van Horn, as attorney for NeXstar Pharmaceuticals, Inc. with regard to this application for extension of the term of U.S. Patent 5,441,745 and to transact all business in the U.S. Patent and Trademark Office in connection therewith.

Applicant hereby submits this application for extension of the patent term under 35 U.S.C. § 156 by providing the following information required by the rules promulgated by the U.S. Patent and Trademark Office (37 C.F.R. § 1.740). For the convenience of the Patent and Trademark Office, the information contained in this application will be presented in a format which will follow the requirements of Section 1.740 of Title 37 of the Code of Federal Regulations.

Applicant hereby advises the Patent and Trademark Office that applications for extension of the term of U.S. Patents Nos. 5,019,369 and 5,435,989 have been filed also based on the regulatory approval of DaunoXome®.

(1) The approved product DaunoXome® contains an aqueous solution of the citrate salt of daunorubicin encapsulated within lipid vesicles (liposomes) composed of a lipid bi-layer of distearoylphosphatidylcholine and cholesterol. The structural formula for daunorubicin citrate is as follows:



(2) The approved product was subject to regulatory review under the Federal Food, Drug and Cosmetic Act Section 505.

(3) The approved product DaunoXome® received permission for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act on April 8, 1996.

(4) The active ingredient in DaunoXome® is the citrate salt of daunorubicin encapsulated within lipid vesicles, which, on information and belief, has not been approved for commercial marketing or use under Section 505 of the Federal Food, Drug and Cosmetic Act prior to the approval of NDA 50704 by the Food and Drug Administration on April 8, 1996. A copy of the insert describing the approved product is attached (Attachment C).

(5) This application for extension of patent term under 35 U.S.C. § 156 is being submitted within the permitted 60-day period pursuant to 37 C.F.R. § 1.720(f), said period will expire on June 7, 1996.

(6) The complete identification of the patent for which a term extension is being sought is as follows:

Inventors: Cary A. Presant, Richard T. Proffitt, Raymond L. Teplitz,  
Lawrence E. Williams, and George W. Tin

Patent No.: 5,441,745

Issue Date: August 15, 1995

Expiration Date: May 28, 2008 (by virtue of a terminal disclaimer filed in  
this patent)

(7) A true copy of the patent is attached (Attachment D).

(8) A copy of the terminal disclaimer filed during the prosecution of U.S. Patent 5,441,745 is attached as Attachment E. No certificate of correction or reexamination certificate has been issued on this patent. Since the patent was granted in August, 1995, no maintenance fees have been due.

(9) U.S. Patent 5,441,745 ('745 patent) claims a method of using DaunoXome®. At least claims 1-5, 6-9, 13 and 15-17 of the '745 patent claim a method of use as follows:

1. A method of placing a chemotherapeutic agent within a tumor for the treatment of the tumor comprising the steps of:

(a) providing small micellular particles of less than 2000 Å comprising chemically pure phospholipid molecules;

(b) incorporating a chemotherapeutic agent within the micellular particles;

and

(c) introducing said micellular particles with said chemotherapeutic agent therein into the bloodstream of the body to place intact said particles and said chemotherapeutic agent in the tumor.

2. A method according to claim 1 wherein said micellular particles constitute distearoyl phosphatidylcholine.

3. A method according to claim 2 wherein said micellular particles are in the form of spherical unilamellar phospholipid vesicles.

4. A method of placing a chemotherapeutic agent within a tumor in a body comprising:

- (a) providing small micellular particles of less than 2000 Å comprising chemically pure phospholipid molecules;
- (b) modifying a portion of said phospholipid micellular particles to provide for the blockage of the reticuloendothelial cells in the body by such modified phospholipid micellular particles;
- (c) initially introducing the modified phospholipid vesicles into the bloodstream of the body to block uptake by the reticuloendothelial cells in the body;
- (d) incorporating a chemotherapeutic agent for treatment of the tumor into a second group of the micellular particles; and
- (e) subsequently introducing the second group of phospholipid micellular particles with said chemotherapeutic agent therein into the bloodstream of the body to place intact said particles and said chemotherapeutic agent within the tumor in the body.

5. A method according to claim 4 wherein said step of modifying a portion of the phospholipid micellular particles to block reticuloendothelial cells in the body comprises incorporating positively charged molecules into the phospholipid.

6. A method of placing a chemotherapeutic agent within a tumor in a body for the diagnosis or treatment of the tumor comprising the steps of:

- (a) providing a first group of micellular particles comprising chemically pure phospholipids having positively charged molecules incorporated therewith;

(b) Introducing such positively charged micellular particles into the bloodstream of the body to block reticulendothelial cells in the body;

(c) providing a second group of small micellular particles of less than 2000 Å comprising chemically pure phospholipid molecules having incorporated therein the chemotherapeutic agent for treatment; and

(d) introducing said second group of micellular particles with the chemotherapeutic agent therein into the bloodstream of the body subsequent to the blocking of reticuloendothelial cells to place intact said particles and said chemotherapeutic agent within the tumor.

7. A method as defined in claim 6 wherein said positively charged molecules incorporated in said first group of micellular particles are amino group derivatives of cholesterol.

8. A method according to claim 7 wherein said positively charged molecules are aminomannose or aminomannitol derivatives of cholesterol.

9. A method according to claim 8 wherein said second group of micellular particles with the chemotherapeutic agent incorporated therein are neutral phospholipid particles.

13. A method of placing a chemotherapeutic agent within a tumor comprising the steps of:

(a) providing small micellular particles of less than 2000 Å comprising chemically pure neutral phospholipids;

(b) adding cholesterol to such chemically pure neutral micellular particles;

(c) incorporating a chemotherapeutic agent into such chemically pure neutral phospholipid micellular particles; and

(d) introducing such small, chemically pure neutral phospholipid micellular particles into the body to place intact said particles and chemotherapeutic agents in the tumor in the body.

15. The method of claims 1, 4, or 5 including the step of incorporating cholesterol into such micellular phospholipid particles or molecules.

16. The method of claim 3 in which distearoyl phosphatidylcholine and cholesterol are included in said particles in a 2:1 molar ratio.

17. The method of claims 1, 4, 6, or 13 in which said micellular particles incorporating said chemotherapeutic agent are phospholipid vesicles and said vesicles are delivered in tact to the tumor cells.

The claims read on a method of using the approved product DaunoXome® because the approved product is a chemotherapeutic agent as used in these claims. Note, for example, the disclosure at column 3, lines 42-45 and 60-64, and column 10, line 63 to col. 11, line 26 of the '745 patent.



(10) The relevant dates and information pursuant to 35 U.S.C. § 156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

Investigational New Drug Application (IND 31,927) for DaunoXome® was filed August 8, 1988 and became effective on September 29, 1988.

New Drug Application for DaunoXome® (NDA 50704) was submitted on February 18, 1993.

New Drug Application for DaunoXome® was approved on April 8, 1996.

(11) A brief description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to DaunoXome® and the dates applicable to these significant activities are set forth in a chronology of events in Attachment F.

(12)(l) Applicant is of the opinion that U.S. Patent 5,441,745 is eligible for extension of the patent term under 35 U.S.C. § 156 because it satisfies all requirements for such extension as follows:

(a) 35 U.S.C. § 156(a) - U.S. Patent 5,441,745 claims a method of using the product DaunoXome®.

(b) 35 U.S.C. § 156(a)(1) - U.S. Patent 5,441,745 has not expired before submission of this application.

(c) 35 U.S.C. § 156(a)(2) - The term of U.S. Patent 5,441,745 has never been extended under 35 U.S.C. § 156(e)(1).

(d) 35 U.S.C. § 156(a)(3) - The application for extension is submitted by the owner of record of the patent in accordance with the requirements of paragraphs (1) through (4) of 35 U.S.C. § 156(d) and the rules of the Patent and Trademark Office.

(e) 35 U.S.C. § 156(a)(4) - The product DaunoXome® has been subjected to a regulatory review period before its commercial marketing or use.

(f) 35 U.S.C. § 156(a)(5)(A) - The commercial marketing or use of the product DaunoXome® after the regulatory review period is the first permitted commercial marketing or use under the provision of the Federal Food, Drug and Cosmetic Act (i.e., Section 505) under which such regulatory review period occurred.

(g) 35 U.S.C. § 156(c)(4) - No other patent has been extended for the same regulatory review period for the product DaunoXome®.

(12)(ii) The length of the extension of patent term of U.S. Patent 5,441,745 claimed by Applicant is that period authorized by 35 U.S.C. § 156(c) which has been calculated to be 237 days. The length of the extension was determined pursuant to 37 C.F.R. § 1.775 as follows:

(a) The regulatory review period under 35 U.S.C. § 156(g)(1)(B) began on September 29, 1988 and ended April 8, 1996, which is a total of 2,748 days, which is the sum of (1) and (2) below:

(1) The period of review under 35 U.S.C. § 156(g)(1)(B)(i), the "Testing Period", began on September 29, 1988 and ended on February 18, 1993, which is 1,603 days; and

(2) The period of review under 35 U.S.C. § 156(g)(1)(B)(ii), the "Approval Period", began on February 18, 1993, and ended on April 8, 1996, which is a total of 1,145 days.

(b) The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in subparagraph 12(ii)(a) above (2,748 days) less:

(1) The number of days in the regulatory review period which were on or before the date on which the patent issued (August 15, 1995) which is 2,511 days; and

(2) The number of days during which applicant did not act with due diligence, which is zero (0) days; and

(3) One-half the number of days determined in sub-paragraph (12)(ii)(a)(1) above after the patent issued which is zero days;

(c) The number of days as determined in sub-paragraph (12)(ii)(b) (237 days) when added to the original term of the patent (May 28, 2008) would result in the date of January 20, 2009;

(d) Fourteen (14) years when added to the date of the NDA approval (April 8, 1996) would result in the date of April 8, 2010;

(e) The earlier date as determined in sub-paragraphs (12)(ii)(c) and (12)(ii)(d) is January 20, 2009;

(f) Since U.S. Patent 5,441,745 issued after September 24, 1984, the period of extension may not exceed five years. Five years when added to the original expiration date of the patent (May 28, 2008) would result in the date of May 28, 2013.

(g) The earlier date as determined by sub-paragraphs (12)(ii)(e) and (12)(ii)(f) is January 20, 2009.

(13) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought.

(14) The prescribed fee for receiving and acting upon this application is attached as a check in the amount of \$1,060.00. The Commissioner is authorized to charge any additional fees required by this application to Deposit Account No. 06-0916.

(15) All correspondence and inquiries may be directed to the undersigned, whose address, telephone number and fax number are as follows:

Charles E. Van Horn

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

1300 I Street, N.W.

Washington, D.C. 20005-3315

Phone: 202-408-4000

Fax: 202-408-4400

(16) Enclosed is a certification that the application for extension of patent term under 35 U.S.C. § 156 including its attachments and supporting papers is being submitted as one original and four (4) copies thereof (Attachment G).

(17) The requisite declaration pursuant to 37 C.F.R. § 1.740(b) is attached (Attachment H).

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

By: Charles E. Van Horn  
Charles E. Van Horn  
Reg. No. 40,266

Date: June 6, 1996

Attachments:

Assignment Documents (Attachment A)

Power of Attorney (Attachment B)

Package Insert for DaunoXome® (Attachment C)

U.S. Patent 5,441,745 (Attachment D)

Copy of Terminal Disclaimer (Attachment E)

Chronology of Regulatory Review Period (Attachment F)

Certification of Copies of Application Papers (Attachment G)

Declaration Pursuant to 37 C.F.R. § 1.740(b) (Attachment H)

LAW OFFICES  
FINNEGAN, HENDERSON,  
FARABOW, GARRETT  
& DUNNER, L.L.P.  
1300 I STREET, N.W.  
WASHINGTON, DC 20005  
202-408-4000

4

PATENT  
Atty. Docket No.: 3036.0006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 5,441,745 )  
)  
Issued: August 15, 1995 )  
)  
To: Cary A. Presant, Richard T. Proffitt, )  
Raymond L. Teplitz, Lawrence E. )  
Williams, and George W. Tin )  
)  
Assignee: NeXstar Pharmaceuticals, Inc. )  
)  
For: METHOD OF DELIVERING )  
MICELLULAR PARTICLES ENCAP- )  
SULATING CHEMOTHERAPEUTIC )  
AGENTS TO TUMORS IN A BODY )

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**CERTIFICATION**

I, CHARLES E. VAN HORN, do hereby certify that this accompanying application for extension of the term of U.S. Patent 5,441,745 under 35 U.S.C. § 158 including its attachments and supporting papers is being submitted as one original and four (4) copies thereof.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

By:

*Charles E. Van Horn*

Charles E. Van Horn  
Reg. No. 40,266

Date: June 6, 1996

LAW OFFICES  
FINNEGAN, HENDERSON,  
FARABOW, GARRETT  
& DUNNER, L.L.P.  
1300 I STREET, N.W.  
WASHINGTON, DC 20005  
202-406-4000

PATENT  
Atty. Docket No.: 3036.0006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 5,441,745 )  
)  
Issued: August 15, 1995 )  
)  
To: Cary A. Presant, Richard T. Proffitt, )  
Raymond L. Teplitz, Lawrence E. )  
Williams, and George W. Tin )  
)  
Assignee: NeXstar Pharmaceuticals, Inc. )  
)  
For: METHOD OF DELIVERING )  
MICELLULAR PARTICLES ENCAP- )  
SULATING CHEMOTHERAPEUTIC )  
AGENTS TO TUMORS IN A BODY )

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**DECLARATION ACCOMPANYING APPLICATION UNDER  
35 U.S.C. § 156 FOR EXTENSION OF PATENT TERM**

I, CHARLES E. VAN HORN, do hereby declare:

I am a patent attorney authorized to practice before the United States Patent and Trademark Office and I have been appointed as an attorney by the Patent Assignee, NeXstar Pharmaceuticals, Inc., with regard to this application for extension of the term of U.S. Patent 5,441,745 and to transact all business in the U.S. Patent and Trademark Office in connection therewith.

I have reviewed and understand the contents of the accompanying application being submitted pursuant to 37 C.F.R. § 1.740.

LAW OFFICES  
FINNEGAN, HENDERSON,  
FARABOW, GARRETT  
& DUNNER, L.L.P.  
1300 I STREET, N.W.  
WASHINGTON, DC 20005  
202-408-4000



I believe that the patent is subject to extension pursuant to 37 C.F.R. § 1.710.

I believe an extension of the length claimed is justified under 35 U.S.C. § 158 and applicable regulations.

I believe the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. § 1.720.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

By: Charles E. Van Horn  
Charles E. Van Horn  
Reg. No. 40,266

Date: June 6, 1996

JUL 10 1996



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 15-22  
Rockville, MD 20857

91  
#95

Dear Mr. Wilson:

The attached application for patent term extension of U.S. Patent No. 5,441,745, which issued August 15, 1995, was filed on June 7, 1996, under 35 U.S.C. § 156.

The assistance of your Office is requested in confirming that the product identified in the application, DaunoXome®, has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

As stated in the application, applications for patent term extension for U.S. Patent Nos. 5,019,369 and 5,435,989 have also been filed. Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156, if elected.

Inquiries regarding this communication should be directed to Karin Tyson at (703) 306-3159.

Hiram A. Bernstein  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Project

cc: Charles E. Van Horn  
Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.  
1300 I Street, N.W.  
Washington, D.C. 20005-3315

kt



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration

Re: DAUNOXOME® (5,441,745)

Docket No. 96E-0286

DEC - 2 1996

Stephen G. Kunin  
Deputy Assistant Commissioner for  
Patent Policy and Projects  
U.S. Patent and Trademark Office  
Box Pat. Ext.  
Assistant Commissioner for Patents  
Washington, D.C. 20231

RECEIVED  
MAY 5 1996  
OFFICE OF PATENTS

02  
#96

Dear Mr. Kunin:

This is in regard to the application for patent term extension for U.S. Patent No. 5,441,745 filed by NeXstar Pharmaceuticals, Inc. under 35 U.S.C. § 156. The human drug product claimed by the patent is DAUNOXOME® (daunorubicin citrate), which was assigned New Drug Application (NDA) No. 50-704.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in Glaxo Operations UK Ltd. v. Quigg, 706 F. Supp. 1224 (E.D. Va. 1989), aff'd, 894 F.2d 392 (Fed. Cir. 1990).

The NDA was approved on April 8, 1996, which makes the submission of the patent term extension application on June 7, 1996, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A), we will then determine the applicable regulatory review period, publish the determination in the Federal Register, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely,

Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs

cc: Charles E. Van Horn  
Finnegan, Henderson, Farabow, Garrett & Dunner  
1300 I Street, N.W.  
Washington, D.C. 20005-3315

JAN 26 1998



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Charles E. Van Horn  
Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.  
1300 I Street, N.W.  
Washington, D.C. 20005-3315

In Re: Patent Term Extension  
Application for  
U.S. Patent No. 5,441,745

67  
#101

#### NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 5,441,745, which claims the method of use of the human drug product DaunoXome® (daunorubicin citrate), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 238 days. U.S. Patent No. 5,441,745 has an original expiration date of May 28, 2008, subject to the provisions of 35 U.S.C. § 41(b). Accordingly, extension of the patent for 238 days will result in an extended expiration date of January 21, 2009.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent and/or a response to the requirement for an election may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration and if the above-identified patent is elected, the Commissioner will issue a certificate of extension, under seal, for a period of 238 days.

The period of extension has been calculated using the FDA determination of the length of the regulatory review period published in the Federal Register of March 21, 1997 (62 Fed. Reg. 13,651). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (1,629 - 1,629) + 1,142 - 904 \\ &= 238 \text{ days}\end{aligned}$$

Since the regulatory review period began September 8, 1988, before the patent issued, August 15, 1995, only that portion of the regulatory review period occurring after the date the patent issued has been considered in the above determination of the length of the extension period. 35 U.S.C. § 156(c). The testing phase of an approved product is defined as the period beginning on the date that an exemption under subsection 505(i) of the Federal Food Drug and Cosmetic Act became effective for the approved product, September 8, 1988, and ending on the date an application for the approved product was initially submitted under section 507, February 22, 1993. Since both of these dates were before the issue date of the patent, none of the testing phase has been considered. The approval phase of a product begins on the date the application for the approved product was initially submitted. For DaunoXome®, this date was February 22, 1993, which was before the issue date of the patent, August 15, 1995. Accordingly, since from February 22, 1993 to August 15, 1995 is 904 days, this period is subtracted from the number of days occurring in the

approval phase according to the FDA determination of the length of the regulatory review period: 1,142 - 904 = 238 days. No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

Neither the 14 year exception of 35 U.S.C. § 156(c)(3) nor the limitations of 35 U.S.C. § 156(g)(6) operate to reduce the period of extension determined above.

It is noted that applicant has also filed applications for patent term extension of U.S. Patent Nos. 5,019,369 and 5,435,989 based upon the regulatory review of the product DaunoXome®. No more than one patent may be extended based upon a regulatory review period of a product. 35 U.S.C. § 156(c)(4). When applications are filed for extension of the terms of different patents based upon the same regulatory review period for a product, the certificate of extension is issued to the patent having the earliest date of issuance unless applicant elects a different patent. Applicant is hereby **REQUIRED TO ELECT** a single patent for extension. In the absence of an election by applicant within ONE MONTH of the date of this notice, and in accordance with 37 CFR 1.785(b), the application for patent term extension in the above-identified patent will be dismissed. (The application for patent term extension for U.S. Patent No. 5,019,369 will be granted.) Accordingly, if the above-identified patent is elected, the Commissioner will issue a certificate of extension, under seal, for a period of 238 days.

Upon issuance of any certificate of extension in the above-identified patent, the following information will be published in the Official Gazette:

U.S. Patent No.	:	5,441,745
Granted	:	August 15, 1995
Original Expiration Date	:	May 28, 2008
Applicant	:	Cary A. Presant et al.
Owner of Record	:	NeXstar Pharmaceuticals, Inc.
Title	:	Method of Delivering Micellular Particles Encapsulating Chemotherapeutic Agents to Tumors in the Body
Classification	:	424/450
Product Trade Name	:	DaunoXome® (daunorubicin citrate)
Term Extended	:	238 days

U.S. Patent No. 5,441,745

Page 3

Expiration Date of Extension : January 21, 2009

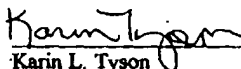
Any correspondence from applicant with respect to this matter should be addressed as follows:

By mail: Assistant Commissioner for Patents  
Box Patent Ext.  
Washington, D.C. 20231

By FAX: (703) 308-6916  
Attn: Special Program Law Office

By hand: One Crystal Park, Suite 520  
2011 Crystal Drive  
Arlington, VA

Telephone inquiries related to this determination should be directed to the undersigned at (703) 306-3159.



Karin L. Tyson  
Senior Legal Advisor  
Special Program Law Office  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects .

cc: Ronald L. Wilson, Director  
Health Assessment Policy Staff  
Office of Health Affairs (HFY-20)  
Food and Drug Administration  
5600 Fishers Lane, Room 15-22  
Rockville, MD 20857

RE: DaunoXome®  
FDA Docket No.: 96E-0286

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

PATENT NO. : 5,441,745  
ISSUED : August 15, 1995  
INVENTOR(S) : Cary A. Presant et al.  
PATENT OWNER : NeXstar Pharmaceuticals, Inc.

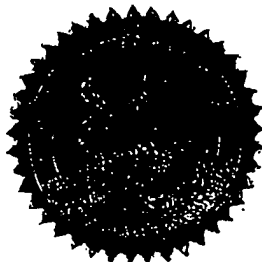
This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

238 days

from May 28, 2008, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the Patent and Trademark Office to be affixed this 27th day of February 1998.

*Bruce A. Lehman*

Bruce A. Lehman  
Assistant Secretary of Commerce and  
Commissioner of Patents and Trademarks



01-17-02 Petition ~~DA~~ ~~AC~~ ~~1~~ ~~2~~ ~~3~~ ~~4~~ ~~5~~ ~~6~~ ~~7~~ ~~8~~ ~~9~~ ~~10~~ ~~11~~ ~~12~~ ~~13~~ ~~14~~ ~~15~~ ~~16~~ ~~17~~ ~~18~~ ~~19~~ ~~20~~ ~~21~~ ~~22~~ ~~23~~ ~~24~~ ~~25~~ ~~26~~ ~~27~~ ~~28~~ ~~29~~ ~~30~~ ~~31~~ ~~32~~ ~~33~~ ~~34~~ ~~35~~ ~~36~~ ~~37~~ ~~38~~ ~~39~~ ~~40~~ ~~41~~ ~~42~~ ~~43~~ ~~44~~ ~~45~~ ~~46~~ ~~47~~ ~~48~~ ~~49~~ ~~50~~ ~~51~~ ~~52~~ ~~53~~ ~~54~~ ~~55~~ ~~56~~ ~~57~~ ~~58~~ ~~59~~ ~~60~~ ~~61~~ ~~62~~ ~~63~~ ~~64~~ ~~65~~ ~~66~~ ~~67~~ ~~68~~ ~~69~~ ~~70~~ ~~71~~ ~~72~~ ~~73~~ ~~74~~ ~~75~~ ~~76~~ ~~77~~ ~~78~~ ~~79~~ ~~80~~ ~~81~~ ~~82~~ ~~83~~ ~~84~~ ~~85~~ ~~86~~ ~~87~~ ~~88~~ ~~89~~ ~~90~~ ~~91~~ ~~92~~ ~~93~~ ~~94~~ ~~95~~ ~~96~~ ~~97~~ ~~98~~ ~~99~~ ~~100~~ ~~101~~ ~~102~~ ~~103~~ ~~104~~ ~~105~~ ~~106~~ ~~107~~ ~~108~~ ~~109~~ ~~110~~ ~~111~~ ~~112~~ ~~113~~ ~~114~~ ~~115~~ ~~116~~ ~~117~~ ~~118~~ ~~119~~ ~~120~~ ~~121~~ ~~122~~ ~~123~~ ~~124~~ ~~125~~ ~~126~~ ~~127~~ ~~128~~ ~~129~~ ~~130~~ ~~131~~ ~~132~~ ~~133~~ ~~134~~ 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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re U.S. Patent No.: 5,532,221  
Issued: July 2, 1996  
To: W. James Wang, et al  
For: Ionically Crosslinked Carboxyl-Containing Polysaccharides for Adhesion Prevention  
From App. No.: 192,336  
Filed: Feb. 4, 1994



RECEIVED  
JAN 23 2002  
OFFICE OF PETITIONS

Box Patent Extension  
Assistant Commissioner for Patents  
Washington, D.C. 20231

Docket No.: L15.1-10292

Sir:

APPLICATION FOR EXTENSION OF THE TERM OF UNITED STATES PATENT NO. 5,532,221 UNDER 35 U.S.C. § 156

Applicant, Lifecore Biomedical, Inc., is a corporation organized under the laws of the State of Minnesota and has a place of business at 3515 Lyman Boulevard, Chaska, Minnesota 55318-3051.

Applicant is the owner of the patent by reason of assignments:

From all inventors to ETHICON INC., recorded in the United States Patent and Trademark Office on April 12, 1994 at Reel/Frame: 6955/0928, and

From ETHICON, INC., to LIFECORE BIOMEDICAL, INC. recorded in the United

States Patent and Trademark Office on October 17, 1994 at Reel/Frame: 7170/0589.

01/23/2002 GTEFFERA 00000167 5532221

01 FC:111

1120.00 CP

Applicant is the holder of the regulatory market approval for the approved product, GYNECARE INTERGEL Adhesion Prevention Solution. GYNECARE and INTERGEL are registered trademarks of Ethicon, Inc., Applicant's distributor for GYNECARE INTERGEL Adhesion Prevention Solution. The product is also identified in some FDA submissions, and in some of Applicant's commercial literature, as INTERGEL Solution. At the time of initial IDE submission, and for some time thereafter, the product was identified as LUBRICOAT Gel.

Pursuant to the provisions of 37 C.F.R. § 1.710-1.777, Applicant hereby applies for an extension of the term of United States Patent No. 5,532,221 under 35 U.S.C. § 156 based on the materials set forth herein and in Exhibits 1- 6 submitted herewith. The requested extension is for a period expiring on **November 16, 2015**.

The Requirements for a complete application for patent term extension are set forth in 37 C.F.R. § 1.740. Those requirements are reproduced below, immediately followed by the required information, a reference to an accompanying document containing the required information, or a statement of non-applicability.

*(a)(1) A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics;*

GYNECARE INTERGEL Adhesion Prevention Solution is a sterile aqueous solution of ferric hyaluronate and sodium hyaluronate. It is prepared by adding ferric chloride to a solution of sodium hyaluronate. The sodium hyaluronate is prepared by neutralization of the acid groups of powder form hyaluronic acid having an average molecular weight in the range of 500,000 to 1,200,000, using an aqueous alkali neutralizing agent. The hyaluronic acid is obtained as a product of a bacterial fermentation.

GYNECARE INTERGEL Adhesion Prevention Solution is indicated for use in patients undergoing open, conservative gynecologic surgery as an adjunct to good surgical technique to reduce post-surgical Adhesions. GYNECARE INTERGEL Adhesion Prevention Solution is also intended to reduce the likelihood of developing moderate or severe postoperative adnexal adhesions in these patients.

*(a)(2) A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred;*

GYNECARE INTERGEL Adhesion Prevention Solution was subject to review under the Federal Food, Drug and Cosmetic act, 35 USC §360(e), as a Class III medical device.

- (a)(3) *An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred;*

GYNECARE INTERGEL Adhesion Prevention Solution received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred on November 16, 2001. A copy of the approval letter is attached as **Exhibit 1.**

- (a)(4) *In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved.*

**Not Applicable**

- (a)(5) *A statement that the application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f) and an identification of the date of the last day on which the application could be submitted;*

This application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f). The last date for on which the application could be submitted is **January 15, 2002.**

- (a)(6) *A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration;*

The names of the inventors are: **W. James Huang, Douglas B. Johns and Richard L. Kroenthal.**

The patent for which an extension is being sought is: **US 5532221.**

The date of issue is: **July 2, 1996**

The date of expiration is: **July 2, 2013**

- (a)(7) *A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings;*

A copy of the patent is attached as **Exhibit 2.**

- (a)(8) *A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or reexamination certificate issued in the patent;*

No disclaimer, certificate of correction, or reexamination certificate has issued in the patent.

A copy of the receipt for the first maintenance fee payment is attached as **Exhibit**

3.

- (a)(9) *A statement that the patent claims the approved product, or a method of using or manufacturing the approved product,*

The patent claims the approved product and a method of using the approved product.

*and a showing which lists each applicable patent claim and demonstrates the manner in which at least one such patent claim reads on:*

- (i) *The approved product, if the listed claims include any claim to the approved product;*

Claim 15 reads on the approved product as shown below.

15. An adhesion preventative	GYNECARE INTERGEL Adhesion Prevention Solution is approved for use as an adhesion preventative.
comprising a sterile non-inflammatory hyaluronic acid fraction having a weight average molecular weight of in the range of from about 550,000 to about 8,000,000	GYNECARE INTERGEL Adhesion Prevention Solution includes a sterile non-inflammatory hyaluronic acid fraction. The hyaluronic acid used to prepare the product have a specification for weight average molecular weight of from 500,000 to 1,200,000. The commercial batches to date have all used hyaluronic acid having an average molecular weight above 550,000.
having carboxyl acid groups which are ionically crosslinked by at least one trivalent cation selected from the group consisting of iron, aluminum and chromium	The carboxyl acid groups of the hyaluronic acid are ionically crosslinked with trivalent iron cations.
wherein from about 60 to about 100 percent of the carboxyl acid groups have been ionically crosslinked by said trivalent cations	About 90 percent of the carboxyl acid groups have been ionically crosslinked with the trivalent iron cations.

and the adhesion preventative has a viscosity of at least 2,500 cps.	The viscosity specification for GYNECARE INTERGEL Adhesion Prevention Solution is 3,000 cps to 28,000 cps.
--	--

(ii) The method of using the approved product, if the listed claims include any claim to the method of using the approved product; and

Claims 1-6 and 11-14 read on the approved product as shown below.

1. A method of reducing the incidence of post-operative adhesion formation in any animal that is susceptible to unwanted adhesion formation following surgery,	GYNECARE INTERGEL Adhesion Prevention Solution is approved for use in patients undergoing open, conservative gynecologic surgery as an adjunct to good surgical technique to reduce post-surgical adhesions. GYNECARE INTERGEL Adhesion Prevention Solution is also intended to reduce the likelihood of developing moderate or severe postoperative adnexal adhesions in these patients.
comprising the step of topically applying as an adhesion preventative an effective amount of a carboxyl-containing polysaccharide, selected from the group consisting of hyaluronic acid and pharmacologically acceptable salts thereof having a weight average molecular weight of in the range of from about 550,000 to about 8,000,000 which has been ionically crosslinked with a trivalent cation provided in an amount sufficient to crosslink in the range of from about 60 to about 100 percent of the carboxyl groups of the carboxyl-containing polysaccharide, to a site of surgical trauma.	GYNECARE INTERGEL Adhesion Prevention Solution meets the formulation requirements of this step as set forth above with respect to claim 1. It is used by topical application of the solution to a surgical site prior to closure of the site.
2. The method of claim 1 wherein the adhesion preventative is derived from hyaluronic acid, or an alkali or alkaline earth metal salt thereof.	GYNECARE INTERGEL Adhesion Prevention Solution is derived from a sodium hyaluronate solution which is in turn derived from hyaluronic acid.

3. The method of claim 2 wherein the adhesion preventative is derived from hyaluronic acid.	See claim 2 statement.
4. The method of claim 2 wherein the adhesion preventative is derived from sodium hyaluronate.	See claim 2 statement.
5. The method of claim 4 wherein the sodium hyaluronate is ionically crosslinked with a trivalent cation selected from the group consisting of iron, aluminum, and chromium provided in an amount sufficient to crosslink in the range of from about 60 to about 100 percent of the carboxyl groups of the sodium hyaluronate.	The carboxyl groups of the sodium hyaluronate used to prepare GYNECARE INTERGEL Adhesion Prevention Solution are ionically crosslinked with trivalent iron cations. About 90 percent of the carboxyl groups have been ionically crosslinked with the trivalent iron cations.
6. The method of claim 5 wherein the sodium hyaluronate is ionically crosslinked with iron.	See claim 5 statement.
11. The method of claim 1 wherein the adhesion preventative is applied directly to the site of surgical trauma in one application.	GYNECARE INTERGEL Adhesion Prevention Solution is typically applied directly to the site of surgical trauma in one application.
12. The method of claim 11 wherein the adhesion preventative is applied during surgery or at the conclusion of surgery prior to closing.	GYNECARE INTERGEL Adhesion Prevention Solution is typically applied at the conclusion of surgery prior to closing.
13. The method of claim 1 wherein the adhesion preventative is made from hyaluronic acid crosslinked with a trivalent cation selected from the group consisting of iron, aluminum and chromium.	GYNECARE INTERGEL Adhesion Prevention Solution is made from hyaluronic acid crosslinked with trivalent iron cations.
14. The method of claim 13 wherein the viscosity of the adhesion preventative is in the range of from about 2,500 cps to about 250,000 cps.	The viscosity specification for GYNECARE INTERGEL Adhesion Prevention Solution is 3,000 cps to 28,000 cps.

*(iii) The method of manufacturing the approved product, if the listed claims include any claim to the method of manufacturing the approved product;*

**Not Applicable**

*(a)(10) A statement beginning on a new page of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:*

*(i) For a patent claiming a human drug, antibiotic, or human biological product:*

*(A) The effective date of the investigational new drug (IND) application and the IND number;*

*(B) The date on which a new drug application (NDA) or a Product License Application (PLA) was initially submitted and the NDA or PLA number; and*

*(C) The date on which the NDA was approved or the Product License issued;*

**Not Applicable**

*(ii) For a patent claiming a new animal drug:*

*(A) The date a major health or environmental effects test on the drug was initiated, and any available substantiation of that date, or the date of an exemption under subsection (j) of Section 512 of the Federal Food, Drug, and Cosmetic Act became effective for such animal drug;*

*(B) The date on which a new animal drug application (NADA) was initially submitted and the NADA number; and*

*(C) The date on which the NADA was approved;*

**Not Applicable**

*(iii) For a patent claiming a veterinary biological product:*

*(A) The date the authority to prepare an experimental biological product under the Virus-Serum-Toxin Act became effective;*

*(B) The date an application for a license was submitted under the Virus-Serum-Toxin Act; and*

*(C) The date the license issued;*

**Not Applicable**

*(iv) For a patent claiming a food or color additive:*

*(A) The date a major health or environmental effects test on the additive was initiated and any available substantiation of that date;*

*(B) The date on which a petition for product approval under the Federal Food, Drug and Cosmetic Act was initially submitted and the petition number; and*

*(C) The date on which the FDA published a Federal Register notice listing the additive for use;*

**Not Applicable**

*(v) For a patent claiming a medical device:*

*(A) The effective date of the investigational device exemption (IDE) and the IDE number, if applicable, or the date on which the applicant began the first clinical investigation involving the device, if no IDE was submitted, and any available substantiation of that date;*

*(B) The date on which the application for product approval or notice of completion of a product development protocol under Section 515 of the Federal Food, Drug and Cosmetic Act was initially submitted and the number of the application; and*

*(C) The date on which the application was approved or the protocol declared to be completed;*

The required description is provided herewith as **Exhibit 4**.

*(a)(11) A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities;*

The required description is provided herewith as **Exhibit 5**.

*(a)(12) A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of extension claimed, including how the length of extension was determined;*

The required statement is provided herewith as **Exhibit 6**.

*(a)(13) A statement that applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought (see § 1.765);*

Applicant hereby acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought.

*(a)(14) The prescribed fee for receiving and acting upon the application for extension (see § 1.20(j));*

The required fee is provided herewith as Check Number 18624. A contingent fee authorization is included in the transmittal to handle any deficiency or overpayment.

and

*(a)(15) The name, address, and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed.*



**In Re: US 5532221**

**Application for Patent Term Extension**

**Title: Ionically Crosslinked Carboxyl-Containing Polysaccharides for Adhesion Prevention**

**Issued: July 2, 1996**

**Page 9**

Please direct inquiries and correspondence relating to this application for patent term extension to:

**Walter J Steinkraus, Reg. No 29592, at the address and phone number associated with Customer Number 490 (currently 6109 Blue Circle Drive Minnetonka MN 55391, phone 952-563-3000, fax 952-563-3001).**

*(b) The application under this section must be accompanied by two additional copies of such application (for a total of three copies).*

With the exception of the Transmittal Letter, check and postcard receipt, all documents submitted this application are being submitted in triplicate

*(c) If an application for extension of patent term is informal under this section, the Office will so notify the applicant. The applicant has two months from the mail date of the notice, or such time as is set in the notice, within which to correct the informality. Unless the notice indicates otherwise, this time period may be extended under the provisions of § 1.136.*

#### *Conclusion*

Based on the foregoing, Applicant respectfully submits that the conditions for extension of the patent term set forth in 37 CFR §1.720(a)-(h) have been satisfied and that Applicant is therefore entitled to an extension of the term of United States Patent No. 5,532,221 for a period to expire 14 years from the date of FDA approval, i.e. on November 16, 2015.

**In Re: US 5532221**

**Application for Patent Term Extension**

**Title: Ionically Crosslinked Carboxyl-Containing Polysaccharides for Adhesion Prevention**

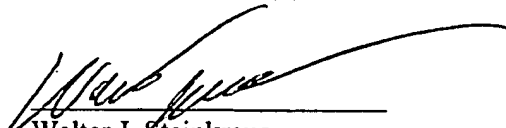
**Issued: July 2, 1996**

**Page 10**

The undersigned is a registered practitioner acting on behalf of the Patent owner. (37 CFR §1.730(b)(2)), and is an attorney of record.

Respectfully submitted,  
Vidas, Arrett & Steinkraus  
Customer Number 490

Dated: January 15, 2002  
Suite 2000  
6109 Blue Circle Drive  
Minnetonka, MN 55343-9131  
Phone: (612) 563-3000  
Facsimile: (612) 563-3001

  
Walter J. Steinkraus  
Registration No. 29592  
Attorney for Applicant



UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS  
UNITED STATES PATENT AND TRADEMARK OFFICE  
WASHINGTON, D.C. 20231  
www.uspto.gov

FEB 19 2002

David T. Read  
Acting Director Health Assessment Policy Staff, CDER  
Food and Drug Administration  
1451 Rockville Pike, HFD-7  
Rockville, MD 20852

Dear Mr. Read:

The attached application for patent term extension of U.S. Patent No. 5,532,221 was filed on January 15, 2002, under 35 U.S.C. § 156.

The assistance of your Office is requested in confirming that the product identified in the application, Gynecare Intergel, has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, or the method of manufacturing or use of such a product, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156.

Inquiries regarding this communication should be directed to the undersigned at (703) 306-3159 (telephone) or (703)308-6916 (facsimile).

Karin Tyson  
Senior Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: VIDAS, ARRETT & STEINKRAUS, P.A.  
6109 BLUE CIRCLE DRIVE  
SUITE 2000  
MINNETONKA, MN 55343-9185

kt



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

DAC



Food and Drug Administration  
Rockville MD 20857

Re: Gynecare Intergel  
Docket No. 02E-0150

The Honorable James. E. Rogan  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office  
Box Pat. Ext.  
P.O. Box 2327  
Arlington, VA 22202

RECEIVED

NOV 0 5 2002

OCT 31 2002

OFFICE OF PETITIONS

Dear Director Rogan:

This is in regard to the application for patent term extension for U.S. Patent No. 5,532,221 filed by Lifecore Medical, Inc. under 35 U.S.C. § 156. The medical device claimed by the patent is Gynecare Intergel, which was assigned premarket approval application (PMA) No. P990015.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in *Glaxo Operations UK Ltd. v. Quigg*, 706 F. Supp. 1224 (E.D. Va. 1989), *aff'd*, 894 F. 2d 392 (Fed. Cir. 1990).

The PMA was approved on November 16, 2001, which makes the submission of the patent term extension application on January 15, 2002, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the *Federal Register*, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely yours,



Jane A. Axelrad

Associate Director for Policy  
Center for Drug Evaluation and Research

cc: Walter J. Steinkraus  
Vida, Arrett & Steinkraus, P.A.  
6109 Blue Circle Drive  
Minnetonka, MN 55391



UNITED STATES PATENT AND TRADEMARK OFFICE

OCT 16 2006

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Dorsey & Whitney LLP  
Intellectual Property Department  
Suite 1500  
50 South Sixth Street  
Minneapolis, MN 55402-1498

In Re: Patent Term Extension  
Application for  
U.S. Patent No. 5,532,221

*[Handwritten signature]*

NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 5,532,221, which claims the medical device Gynecare® Intergel, is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 867 days.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Director will issue a certificate of extension, under seal, for a period of 867 days.

The period of extension has been calculated using the Food and Drug Administration determination of the length of the regulatory review period published in the Federal Register of April 2, 2003 (68 Fed. Reg. 16061). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (1,453 - 474) + 985 \\ &= 1,475 \text{ days (4.0 years)}\end{aligned}$$

Since the regulatory review period began March 17, 1995, before the patent issued (July 2, 1996), only that portion of the regulatory review period occurring after the date the patent issued has been considered in the above determination of the length of the extension period 35 U.S.C. § 156(c). (From March 17, 1995, to and including July 2, 1996, is 474 days; this period is subtracted for the number of days occurring in the testing phase according to the FDA determination of the length of the regulatory review period.). No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

However, the 14 year exception of 35 U.S.C. § 156(c)(3) operates to limit the term of the extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the approved product plus any patent term extension cannot exceed fourteen years. The period of extension calculated above, 1,475 days, would extend the patent from July 2, 2013 to July 16, 2017, which is beyond the 14-year limit (the approval date is November 16, 2001, thus, the 14 year limit is November 16, 2015). The period of extension is thus limited to 867 days, by operation of 35 U.S.C. § 156(c)(3). Accordingly, the period of extension is the number of days to extend the term of the patent from its original expiration date, July 2, 2013, to and including November 16, 2015, or 867 days.

The limitations of 35 U.S.C. 156(g)(6) do not operate to further reduce the period of extension determined above.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.: 5,532,221  
Granted: July 2, 1996


Original Expiration Date<sup>1</sup>: July 2, 2013  
Applicant: W. James Huang, et al.  
Owner of Record: Lifecare Biomedical, Inc.  
Title: Ionically Crosslinked Carboxyl-Containing Polysaccharides for Adhesion Prevention  
Product Trade Name: Gynecare® Intergel  
Term Extended: 867 days  
Expiration Date of Extension: November 16, 2015

It is noted that a change of power of attorney and change in correspondence address were filed in the above captioned patent. Therefore, all correspondence regarding the patent term extension for U.S. Patent No. 5,532,221 is now being mailed to the address associated with customer number 25763.

Any correspondence with respect to this matter should be addressed as follows:

By mail: Mail Stop Patent Ext. Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450.  
By FAX: (571) 273-7755

Telephone inquiries related to this determination should be directed to the undersigned at (571) 272-7755.

  
Mary C. Till  
Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

cc: Office of Regulatory Policy  
HFD - 7  
5600 Fishers Lane (Rockwall II Rm. 1101)  
Rockville, MD 20857  
Attention: Beverly Friedman

RE: Gynecare® Intergel  
FDA Docket No.: 02E-0150

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<sup>1</sup>Subject to the provisions of 35 U.S.C. § 41(b).



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Dorsey & Whitney LLP  
Intellectual Property Department  
Suite 1500  
50 South Sixth Street  
Minneapolis, MN 55402-1498

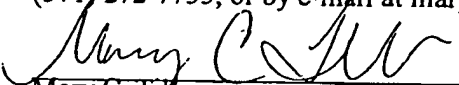
In Re: Patent Term Extension  
Application for  
U.S. Patent No. 5,532,221

MAR 20 2007

Dear Mr. Rothenberger :

A certificate under 35 U.S.C. § 156 is enclosed extending the term of U.S. Patent No. 5,532,221 for a period of 867 days. While a courtesy copy of this letter is being forwarded to the Food and Drug Administration (FDA), you should directly correspond with the FDA regarding any required changes to the patent expiration dates set forth in the Patent and Exclusivity Data Appendix of the Orange Book (Approved Drug Products with Therapeutic Equivalence Evaluations) or in the Patent Information set forth in the Green Book (FDA Approved Animal Drug Products). Effective August 18, 2003, patent submissions for publication in the Orange Book and Docket \*95S-0117 need to be submitted on form FDA-3542 which may be downloaded from FDA's Electronic Forms Download Website: <http://www.fda.gov/opacom/morechoices/fdaforms/default.html> (<http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3542.pdf>).

Inquiries regarding this communication should be directed to the undersigned by telephone at (571) 272-7755, or by e-mail at [mary.till@uspto.gov](mailto:mary.till@uspto.gov).

  
Mary C. Till  
Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: Office of Regulatory Policy  
HFD-7  
5600 Fishers Lane (Rockwall II Rm 1101)  
Rockville, MD 20857

RE: Gynecare® Intergel  
FDA Docket No.: 02E-0150

Attention: Beverly Friedman

UNITED STATES PATENT AND TRADEMARK OFFICE

(12) CERTIFICATE EXTENDING PATENT TERM  
UNDER 35 U.S.C. § 156

(68) PATENT NO. : 5,532,221  
(45) ISSUED : July 2, 1996  
(75) INVENTOR : W. James Huang, et al.  
(73) PATENT OWNER : Lifecare Biomedical, Inc.  
(95) PRODUCT : Gynecare® Intergel

This is to certify that an application under 35 U.S.C. § 156 has been filed in the United States Patent and Trademark Office, requesting extension of the term of U.S. Patent No. 5,532,221 based upon the regulatory review of the product Gynecare® Intergel by the Food and Drug Administration. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

(94) 867 days

from July 2, 2013, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the United States Patent and Trademark Office to be affixed this 19th day of March 2007.

  
Jon W. Dudas  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office





08/268,734

DAC/8  
CC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: REDDY1.3 EXT

In re Patent of: ) Conf. No.: 4565  
)  
Vermuri REDDY et al )  
)  
Patent No.: 5,639,639 )  
)  
Issued: June 17, 1997 ) Washington, D.C.  
)  
For: RECOMBINANT HETERODIMERIC ) December 7, 2004  
HUMAN FERTILITY HORMONES, )  
AND METHODS, CELLS, )  
VECTORS AND DNA FOR THE )  
PRODUCTION THEREOF )

RECEIVED  
DEC 10 2004  
OFFICE OF PETITIONS

APPLICATION FOR EXTENSION OF PATENT TERM

Honorable Commissioner for Patents  
U.S. Patent and Trademark Office  
2011 South Clark Place  
Customer Window, Mail Stop Patent Ext.  
Crystal Plaza Two, Lobby, Room 1B03  
Arlington, VA 22202

Sir:

In accordance with 35 U.S.C. §156, patentee, Genzyme Corporation, through the undersigned attorney, hereby applies for extension of the term of the above-identified patent.

Following is the information required by 37 C.F.R. §1.740.

(a) (1) The approved product is lutropin alfa also known as recombinant human luteinizing hormone (r-hLH).

Lutropin alfa is a water soluble glycoprotein consisting of two non-covalently linked subunits - designated  $\alpha$  and  $\beta$  - consisting of 92 and 121 amino acid residues, respectively,

12/08/2004 JBALINAM 00000051 5639639

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1120.00 DP

In re of Patent ~~No.~~ 5,639,639

with carbohydrate moieties linked to Asn-52 and Asn-78 (on the  $\alpha$  subunit) and Asn-30 (on the  $\beta$  subunit). The full amino acid sequence of the  $\alpha$  and  $\beta$  subunits of lutropin alfa is as follows:

$\alpha$  subunit:

Ala	Pro	Asp	Val	Gln	Asp	Cys	Pro	Glu	Cys	Thr	Leu	Gln	Glu	Asn	Pro	
1				5					10					15		
Phe	Phe	Ser	Gln	Pro	Gly	Ala	Pro	Ile	Leu	Gln	Cys	Met	Gly	Cys	Cys	
			20					25					30			
Phe	Ser	Arg	Ala	Tyr	Pro	Thr	Pro	Leu	Arg	Ser	Lys	Lys	Thr	Met	Leu	
		35					40					45				
Val	Gln	Lys	Asn	Val	Thr	Ser	Glu	Ser	Thr	Cys	Cys	Val	Ala	Lys	Ser	
	50					55					60					
Tyr	Asn	Arg	Val	Thr	Val	Met	Gly	Gly	Phe	Lys	Val	Glu	Asn	His	Thr	
65					70					75					80	
Ala	Cys	His	Cys	Ser	Thr	Cys	Tyr	Tyr	His	Lys	Ser					
		115					120									

$\beta$  subunit:

Ser	Arg	Glu	Pro	Leu	Arg	Pro	Trp	Cys	His	Pro	Ile	Asn	Ala	Ile	Leu	
1				5					10					15		
Ala	Val	Glu	Lys	Glu	Gly	Cys	Pro	Val	Cys	Ile	Thr	Val	Asn	Thr	Thr	
			20					25					30			
Ile	Cys	Ala	Gly	Tyr	Cys	Pro	Thr	Met	Met	Arg	Val	Leu	Gln	Ala	Val	
		35					40					45				
Leu	Pro	Pro	Leu	Pro	Gln	Val	Val	Cys	Thr	Tyr	Arg	Asp	Val	Arg	Phe	
	50					55					60					
Glu	Ser	Ile	Arg	Leu	Pro	Gly	Cys	Pro	Arg	Gly	Val	Asp	Pro	Val	Val	
65					70					75					80	
Ser	Phe	Pro	Val	Ala	Leu	Ser	Cys	Arg	Cys	Gly	Pro	Cys	Arg	Arg	Ser	
				85					90					95		

In re of Patent No. 5,639,639

Thr Ser Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr Cys Asp His  
100 105 110

Pro Gln Leu Ser Gly Leu Leu Phe Leu  
115 120

Asn: N-glycosylation site

(a)(2) The product was approved under Section 505(b) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §355(b)).

(a)(3) The product received permission for commercial marketing or use under Section 505(b) of the Federal Food, Drug and Cosmetic Act on October 8, 2004.

(a)(4) As the present product is a human biological product and not a drug product (as those terms are used in the Federal Food, Drug and Cosmetic Act and the Public Health Service Act), 37 C.F.R. §1.740(a)(4) is not applicable.

(a)(5) The present application is being submitted within the sixty-day period permitted for submission pursuant to 37 C.F.R. §1.720(f). It is required that the application be filed within sixty days following the date of the FDA approval letter of October 8, 2004. The sixty-day period expires on December 7, 2004, which is, thus, the last date on which the application can be filed.

(a)(6) The patent for which an extension is being sought is U.S. patent 5,639,639, of which the inventors are Vermuri B. Reddy, Nancy Hsiung, Anton K. Beck, and Edward

In re of Patent No. 5,639,639

George Bernstine. The date of issue was June 17, 1997.

Because of the filing of a terminal disclaimer, the date of expiration is June 20, 2006.

(a)(7) A copy of patent 5,639,639 is attached hereto as Exhibit A, including the entire specification (including claims and drawings).

(a)(8) Attached hereto as Exhibit B is a copy of the Terminal Disclaimer filed during the prosecution of the applications that led to the issuance of the '639 patent. Please note that the Terminal Disclaimer was filed in Application No. 07/515,481. The '639 application issued from Application No. 08/268,734, which was a file-wrapper continuation of said Application No. 07/515,481. Thus, the Terminal Disclaimer of Exhibit B is effective with respect to the '639 patent. Also attached hereto as Exhibits C and D are copies of receipts of maintenance fee payments establishing that the first and second maintenance fees were timely paid with respect to this patent.

(a)(9) The patent claims a method of manufacturing the approved product. Each claim of the patent which claims a method of manufacturing the approved product is identified as claims 1, 3, 6 and 8. Attached hereto as Exhibit E are portions of the original NDA submitted during the FDA approval process. Exhibit E includes pages numbered 036-045. These

documents are a summary of the chemistry and the manufacturing process of the approved product. This manufacturing process of the approved product falls within the scope of claim 1 of the '639 patent. Also part of Exhibit E as page 096 is Table BAA-1 showing batch analysis results. Exhibit E also includes pages numbered 242-264, which relate to the development genetics that led to the approved product of the '639 product.

The following showing demonstrates the manner in which claim 1 reads on the method of manufacturing the approved product.

Patent Claim

A process for producing biologically active heterodimeric human fertility hormone selected from the group consisting of human chorionic gonadotropin, human luteinizing hormone and human follicle stimulating hormone, comprising:

Approved Product

Page 036 of Exhibit E states that the active substance that is produced is recombinant human luteinizing hormone, which is one of the products listed in the Markush group in the preamble of claim 1. That it is biologically active is evident from the last line of the table on page 096 of Exhibit E, which shows a specific bioactivity in the various batches running between 25,819 to 31,229 IU/mg. Thus, as the hLH can be measured in international units, biologically active hLH is produced by the method.

transforming a eukaryotic cell

See page 248 of Exhibit E under the heading "Preparation of the production cell line", where it states, "The employed CHO cell line was co-transfected with two expression plasmids, encoding the  $\alpha$ - and  $\beta$ -subunits." Thus, it is clear that CHO cells were transformed. Page 041 of Exhibit E, under section 3.4.1.4.2, defines CHO cells as Chinese hamster ovary cells. The Chinese hamster is a mammal, and it is well known that all mammalian cells are eukaryotic.

with at least one vector constructed so as to insert into said cell DNA coding for each of the two subunits of the hormone,

As seen in the above-quoted portion from page 248 of Exhibit E, the CHO cell line was co-transfected with two expression plasmids encoding the  $\alpha$ - and  $\beta$ -subunits. The claimed "at least one vector" encompasses two vectors. That the vectors were constructed so as to insert the DNA of the subunits into the cell is evident from the fact that the cell lines ultimately produce both subunits of hLH so as to produce a biologically active product, as can be seen from page 096 of Exhibit E, discussed above.

the translation of the DNA of each said subunit being controlled by a separate promoter; and

That each subunit is controlled by a separate promoter is evident from the third paragraph on page 242 of Exhibit E. The  $\alpha$ -genomic fragment was inserted into the expression vector downstream of and juxtaposed to the mouse metallothionein (MMT) gene promoter. Later, it says that the second vector was of similar design but contained the  $\beta$ -hLH cDNA in place of the  $\alpha$ -subunit gene and the selectable ODC gene in place of the DHFR gene. Thus, it is apparent from the fact that a similar design was used, that the second vector also contains the MMT gene promoter. This is also evidenced by the restriction enzyme map of pH $\alpha$ DHFR at page 257 of Exhibit E, clearly showing that an MMT-1 promoter is present in this plasmid, and the restriction enzyme map of pHLH $\beta$ ODC on page 260 of Exhibit E, which shows that the  $\beta$ -subunit is also controlled by an MMT promoter. Thus, each subunit is being controlled by a separate promoter.

culturing said cell under conditions appropriate to permit expression of the hormone therefrom,

Reference is made to section 3.4.1.4.3.1 on page 042 of Exhibit E, teaching the conditions of cell culture and the expression of r-hLH therefrom (see the last line of Figure 2 on page 045 of Exhibit E.

wherein said eukaryotic cell is one which permits appropriate post-translational modification of the subunits so produced such that the formed protein is biologically active.

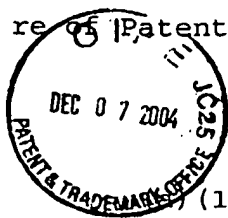
That post-translational modification occurs is evident from the glycosylation pattern and cysteine bridges in the subunits, discussed on pages 036-038 of Exhibit E. Note the statement in the fourth paragraph from the end on page 038, which states, "Correct pairing of the cysteines in the recombinant molecules can be assumed as the *in vivo* bioactivity and immunoactivity of the r-hLH molecule are maintained." Thus, it is apparent that there is post-translational modification and that the formed protein is biologically active.



In re of Patent No. 5,639,639

(a)(10)(i) The Investigational New Drug (IND) application was submitted on December 8, 1993, and received on December 10, 1993. The FDA letter acknowledging receipt was mailed on December 15, 1993, stating that studies may begin 30 days after the date of receipt, i.e., January 9, 1994. The IND application was assigned IND number 44,108. The New Drug Application was initially submitted on April 30, 2001, was received on May 1, 2001, and was assigned NDA number 21-322. The NDA was approved on October 8, 2004.

In re Patent No. 5,639,639



(11) The following is a brief description of significant activities undertaken by the marketing applicant during the applicable review period:

IND submitted - protocols for Phase II/III Study 6253 and Study 6905	December 8, 1993
FDA Action Letter and Acknowledgement of Receipt	December 15, 1993
Study 6253 Complete	April 1995
Study 6905 Complete	July 1997
IND Amendment - Protocol for Phase III Study 21008	July 1, 1999
IND Amendment - Protocol for Extension Study 21415	January 31, 2000
Study 21008 Complete	September 2000
Pre-NDA meeting - Study Results Presented	December 12, 2000
NDA Submitted	April 30, 2001
NDA Received	May 1, 2001
Study 21415 Complete	August 2001
Not Approvable Letter	March 1, 2002
NDA Amendment - Report for Study 21415 Submitted	April 28, 2003
Reproductive Health Drugs Advisory Committee	September 30, 2003
NDA Amendment - Phase IV Protocol	October 5, 2004
Approval Letter	October 8, 2004

In re of Patent No. 5,639,639

(a) (14) Attached hereto is PTO Form 2038, Credit Card Payment Form, authorizing payment in the amount of \$1,120.00 in accordance with 37 C.F.R. §1.20(j)(1) for receiving and acting upon the application for extension.

(a) (15) The name, address and telephone number of the person to whom inquiries and correspondence relating to the present application are to be directed is as follows:

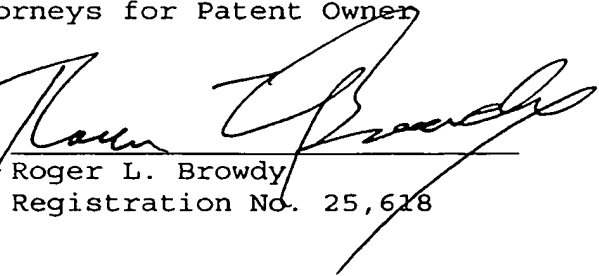
Roger L. Browdy  
BROWDY AND NEIMARK, P.L.L.C.  
624 Ninth Street, N.W.  
Suite 300  
Washington, D.C. 20001-5303

Telephone: 202-628-5197  
Facsimile: 202-737-3528.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Patent Owner

By



Roger L. Browdy  
Registration No. 25,618

RLB:rd  
Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528  
G:\BN\S\Ser1\Reddy1.3Ext\AppExtTime.doc



UNITED STATES PATENT AND TRADEMARK OFFICE

OCT - 6 2005

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

Office of Regulatory Policy  
HFD - 13  
5600 Fishers Lane,  
Rockville, MD 20857

Attention: Claudia Grillo

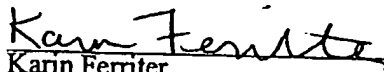
Dear Ms. Axelrad:

The attached application for patent term extension of U.S. Patent No. 5,639,639 was filed on December 7, 2004, under 35 U.S.C. § 156.

The assistance of your Office is requested in confirming that the product identified in the application, lutropin alfa (recombinant human luteinizing hormone) (Luveris®), has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, or a method of manufacturing or use of such a product, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156, but it is noted that the listing of CDER Drug and Biologic Approvals for Calendar Year 2004 lists the approval of lutropin alfa (Luveris®) as a New Drug Application, not a Biologic License Application approval, and the approval of a new formulation, not a new chemical entity. The indication that the NDA was approved as a new formulation suggests that the active ingredient in Luveris® was previously approved, and further information about any prior approvals of lutropin alfa is requested.

Inquiries regarding this communication should be directed to the undersigned at (571) 272-7744 (telephone) or (571) 273-7744 (facsimile).



Karin Ferriter  
Senior Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: Roger L. Browdy  
Browdy and Neimark, P.L.L.C.  
624 Ninth Street, NW  
Suite 300 Washington DC 20001-5303

Enclosure: CDER Drug and Biologic Approvals for Calendar Year 2004 (five pages)



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Roger L. Browdy  
Browdy and Neimark, P.L.L.C.  
624 Ninth Street, NW  
Suite 300  
Washington, DC 20001-5303

In re: Patent Term Extension  
Application for  
U.S. Patent No. 5,639,639

JAN 29 2007

NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 5,639,639, which claims the human biological product LUVERIS® (lutropin alfa), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 5 years.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Director will issue a certificate of extension, under seal, for a period of 5 years.

The period of extension has been calculated using the Food and Drug Administration determination of the length of the regulatory review period published in the Federal Register of June 13, 2006 (71 Fed. Reg. 34136). Under 35 U.S.C. § 156(c):

Period of Extension =  $\frac{1}{2}$  (Testing Phase) + Approval Phase  
=  $\frac{1}{2}$  (2670 - 1256) + 1257  
= 1964 days (5.4 years)

Since the regulatory review period began January 9, 1994, before the patent issued (June 17, 1997), only that portion of the regulatory review period occurring after the date the patent issued has been considered in the above determination of the length of the extension period 35 U.S.C. § 156(c). (From January 9, 1994 to and including June 17, 1997 is 1256 days; this period is subtracted for the number of days occurring in the testing phase according to the FDA determination of the length of the regulatory review period.) No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

The five year limitation of 35 U.S.C. § 156(g)(6)(A) applies in the present situation because the patent was issued after the date of enactment of 35 U.S.C. § 156. Since the period of extension calculated under 35 U.S.C. § 156(c) for the patent cannot exceed five years under 35 U.S.C. § 156(g)(6)(A), the period of extension will be for five years.

The 14 year limitation of 35 U.S.C. § 156(c)(3) does not operate to further reduce the period of extension determined above.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.: 5,639,639

Granted: June 17, 1997

Original Expiration Date<sup>1</sup>: June 20, 2006  
Applicant: Vermuri B. Reddy, et al.  
Owner of Record: Genzyme Corporation  
Title: RECOMBINANT HETERODIMERIC HUMAN  
FERTILITY HORMONES AND METHODS,  
CELLS, VECTORS AND DNA FOR THE  
PRODUCTION THEREOF  
Product Trade Name: LUVERIS® (lutropin alfa)  
Term Extended: 5 years  
Expiration Date of Extension: June 20, 2011

Any correspondence with respect to this matter should be addressed as follows:

By mail: Mail Stop Hatch-Waxman PTE                      By FAX: (571) 273-7754  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450.

Telephone inquiries related to this determination should be directed to the undersigned at (571) 272-7754.



Kathleen Kahler Fonda  
Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: Office of Regulatory Policy  
HFD - 7  
5600 Fishers Lane (Rockwall II Rm. 1101)  
Rockville, MD 20857

RE: LUVERIS® (lutropin alfa)  
FDA Docket No.: 2006E-0026

Attention: Beverly Friedman

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<sup>1</sup>Subject to the provisions of 35 U.S.C. § 41(b).



UNITED STATES PATENT AND TRADEMARK OFFICE

APR 11 2007

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)


Roger L. Browdy  
Browdy and Neimark, P.L.L.C.  
624 Ninth Street, NW  
Suite 300  
Washington, DC 20001-5303

In Re: Patent Term Extension  
Application for  
U.S. Patent No. 5,639,639

Dear Mr. Browdy :

A certificate under 35 U.S.C. § 156 is enclosed extending the term of U.S. Patent No. 5,639,639 for a period of 5 years. While a courtesy copy of this letter is being forwarded to the Food and Drug Administration (FDA), you should directly correspond with the FDA regarding any required changes to the patent expiration dates set forth in the Patent and Exclusivity Data Appendix of the Orange Book (Approved Drug Products with Therapeutic Equivalence Evaluations) or in the Patent Information set forth in the Green Book (FDA Approved Animal Drug Products). Effective August 18, 2003, patent submissions for publication in the Orange Book and Docket \*95S-0117 need to be submitted on form FDA-3542 which may be downloaded from FDA's Electronic Forms Download Website:  
<http://www.fda.gov/opacom/morechoices/fdaforms/default.html>  
(<http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3542.pdf>).

Inquiries regarding this communication should be directed to the undersigned by telephone at (571) 272-7755, or by e-mail at [mary.till@uspto.gov](mailto:mary.till@uspto.gov).

  
Mary C. Till  
Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: Office of Regulatory Policy  
HFD-7  
5600 Fishers Lane (Rockwall II Rm 1101)  
Rockville, MD 20857

RE: LUVERIS® (lutropin alfa)  
FDA Docket No.: 2006E-026

Attention: Beverly Friedman

# UNITED STATES PATENT AND TRADEMARK OFFICE

## (12) CERTIFICATE EXTENDING PATENT TERM UNDER 35 U.S.C. § 156

(68) PATENT NO. : 5,639,639  
(45) ISSUED : June 17, 1997  
(75) INVENTOR : Vermuri B. Reddy, et al.  
(73) PATENT OWNER : Genzyme Corporation  
(95) PRODUCT : LUVERIS® (lutropin alfa)

This is to certify that an application under 35 U.S.C. § 156 has been filed in the United States Patent and Trademark Office, requesting extension of the term of U.S. Patent No. 5,639,639 based upon the regulatory review of the product LUVERIS® (lutropin alfa) by the Food and Drug Administration. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

(94) 5 years

from June 20, 2006, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the United States Patent and Trademark Office to be affixed this 3rd day of April 2007.

  
Jon W. Dudas  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office



## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent of

Bengt ÅGERUP

Patent No. 5,827,937

Issued: October 27, 1998

FOR: POLYSACCHARIDE GEL  
COMPOSITION

MAIL STOP: PATENT EXTENSION

RECEIVED

FEB 10 2004

REEXAM UNIT

VIA HAND-CARRY TO USPTO**TRANSMITTAL LETTER FOR APPLICATION FOR EXTENSION  
OF PATENT TERM UNDER 35 U.S.C. § 156**Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Enclosed is an Application for Extension of Patent Term Under 35 U.S.C. § 156 (an original and three copies) for the above-identified patent.

Also enclosed with the original and each of the three copies are the following documents:

1. Attachment A (Copy of Product Information About RESTYLANE® Injectable Gel)
2. Attachment B (Copy of Approval Letter from the FDA for RESTYLANE® Injectable Gel)
3. Attachment C (Copy of U.S. Patent No. 5,827,937)
4. Attachment D (Copy of Statutory Disclaimer of Claim 4 for U.S. Patent No. 5,827,937)
5. Attachment E (Copies of Maintenance Fee Statement for U.S. Patent No. 5,827,937)
6. Attachment F (Copy of Recorded Assignment Document for U.S. Patent No. 5,827,937)
7. Attachment G (Copy of Authorization from Q-MED Scandinavia to Q-MED AB to Rely Upon Activities of Q-MED Scandinavia Before the FDA in Making Its Applications for Extension and Extension of Patent Term)

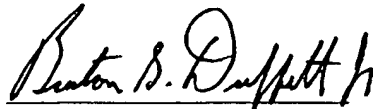
8. Attachment H (Copy of Power of Attorney).

Please charge the requisite fee in the amount of \$1,120.00 to Deposit Account No. 02-4800.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, LLP



Benton S. Duffett, Jr.  
Registration No. 22,030

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(838) 838-6620

Date: February 10, 2004

Patent  
Attorney's Docket No. 003300-356

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

*In re* Patent of

Bengt ÅGERUP

Patent No.: 5,827,937

Issued: October 27, 1998

For: POLYSACCHARIDE GEL  
COMPOSITION

**MAIL STOP: PATENT EXTENSION**

RECEIVED

FEB 10 2004

REEXAM UNIT

# APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. § 156

## MAIL STOP: PATENT EXTENSION

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the provisions of 35 U.S.C. § 156 and 37 C.F.R. § 1.710 *et seq.*, the owner of record of U.S. Patent No. 5,827,937 requests that the term of this patent be extended by 879 days to expire on **December 12, 2017**.

U.S. Patent No. 5,827,937 was filed on July 17, 1995 and issued on October 27, 1998 for "POLYSACCHARIDE GEL COMPOSITION," listing Bengt Ågerup as the sole inventor. The term of U.S. Patent No. 5,827,937 will expire, unless extended, on July 17, 2015 (*i.e.*, twenty years from the date on which the application for the patent was filed in the United States).

Q-MED AB, a Swedish corporation, is the assignee of the entire right, title and interest in U.S. Patent No. 5,827,937, granted to Bengt Ågerup, on October 27, 1998 for POLYSACCHARIDE GEL COMPOSITION, by virtue of an assignment from the inventors to Q-MED AB, Upsala, Sweden, recorded on September 8, 1997 at Reel 8741, Frame 0942.

Q-MED AB submits this application for extension of the patent term of U.S. Patent No. 5,827,937 by providing the following information in accordance with 35 U.S.C. § 156 and 37 C.F.R. § 1.710 *et seq.*, and follows the numerical format set forth in 37 C.F.R. §1.740(a)(1)-(15)

**(1) COMPLETE IDENTIFICATION OF PRODUCT**

The product presently subject to regulatory review is RESTYLANE® Injectable Gel (trade name). Product information from the U.S. Food and Drug Administration website regarding RESTYLANE® Injectable Gel is attached at ATTACHMENT A.

RESTYLANE® Injectable Gel contains 20 mg/ml of non-animal stabilized hyaluronic acid (hereinafter "NASHA") in buffered physiological sodium chloride solution pH 7. RESTYLANE® Injectable Gel is a sterile, transparent, viscous gel supplied in a 1 ml disposable glass syringe filled with 0.4 or 0.7 ml gel. The syringe is equipped with a tip cap, finger grip, plunger stopper and plunger rod. The product is for single use only. A sterile 30G needle is supplied in the package.

Hyaluronic acid is a polymer containing alternating units of glucuronic acid (GlcUA) and N-acetylglucosamine (GlcNAc). NASHA is a generic name for the stabilized forms of Hyaluronic Acid (hereinafter "HA") from Q-MED. The HA in RESTYLANE® Injectable Gel is stabilized by adding a minimum amount of 1,4-butanediol diglycidyl ether to allow formation of a 3-dimensional HA molecular network (gel). The patented chemical stabilizing process used by Q-MED does not change the polyanionic character of the polysaccharide chain. As only about 1% of the polysaccharide has been stabilized the substance remains biocompatible.

Hyaluronic acid belongs to a group of very few substances, which are identical in all living organisms. It is a natural polysaccharide that is present throughout the tissues of the body.

It occurs as an important structural element in the skin and in subcutaneous and connective tissues as well as in the synovial tissue and fluid. RESTYLANE® Injectable Gel is biologically almost identical to hyaluronic acid and is degraded in the body by the same metabolic pathway as endogenous hyaluronic acid. RESTYLANE® Injectable Gel acts by adding volume to the tissue, thereby restoring the skin contours to the desired level of correction. RESTYLANE® Injectable Gel is naturally integrated into the tissue and will in time undergo isovolemic degradation.

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

**(2) IDENTIFICATION OF FEDERAL STATUTE/PROVISION OF LAW**

RESTYLANE® Injectable Gel is subject to regulatory review under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355), as a Class III medical device.

Application For Extension Of  
Patent Term Under 35 U.S.C. § 156  
for U.S. Patent No. 5,827,937  
Attorney Docket No.: 003300-356

**(3) DATE ON WHICH PRODUCT RECEIVED PERMISSION FOR COMMERCIAL  
MARKETING OR USE**

RESTYLANE® Injectable Gel received permission for commercial marketing under  
Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355) on **December 12,**  
**2003.** A copy of the approval letter is attached as ATTACHMENT B.



**(4) IDENTIFICATION OF EACH ACTIVE INGREDIENT**

37 C.F.R. §1.740(a)(4) requires that in the case of a drug product, "an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved."

RESTYLANE® Injectable Gel is a Class III medical device, not a drug product. Moreover, RESTYLANE® Injectable Gel does not contain any active ingredient. Accordingly, this section is not applicable.

**(5) TIME PERIOD FOR SUBMITTING APPLICATION**

This application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f). Specifically, this application is being submitted within the sixty-day period "beginning on the date the product first received permission for commercial marketing or use under the provisions of law under which the applicable regulatory review period occurred."

RESTYLANE® Injectable Gel received permission for commercial marketing under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355) on December 12, 2003. A copy of the approval letter is attached at ATTACHEMENT B. Sixty days from December 12, 2003 would be February 10, 2004.

Thus, the last day on which this application could be submitted is **February 10, 2004.**

**(6) IDENTIFICATION OF PATENT**

The patent for which patent term extension is being sought is U.S. Patent No. 5,827,937, which was filed on July 17, 1995 and issued on October 27, 1998 for "POLYSACCHARIDE GEL COMPOSITION," listing Bengt Ågerup as the sole inventor.

The term of U.S. Patent No. 5,827,937 will expire, unless extended, on July 17, 2015 (twenty years from the date on which the application for the patent was filed in the United States).

**(8) OTHER PATENT DOCUMENTS**

A copy of the statutory disclaimer of Claim 4 is attached as ATTACHMENT D.

The records of the undersigned do not indicate that any other disclaimer, certificate of correction or reexamination certificate were issued in U.S. Patent No. 5,827,937.

The fourth-year maintenance fee has been paid, and a copy of the maintenance fee statement (from the U.S. Patent & Trademark Office Web site) verifying the payment is attached as ATTACHMENT E.

A copy of the recorded Assignment documents (from the records of the U.S. Patent and Trademark Office) are attached as ATTACHMENT F.

**(9) CLAIM(S) COVERING THE PRODUCT**

The claims of U.S. Patent No. 5,827,937 cover the approved product, RESTYLANE®  
Injectable Gel, as well as a method of manufacturing the approved product.

As required, Applicants provide a showing below, which lists each applicable patent  
claim and demonstrates the manner in which each of the following claims reads upon the  
approved product and the method of manufacturing the approved product.

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>1. A process for preparing a cross-linked biocompatible polysaccharide gel composition, which process comprises the following steps:</p> <p>(i) forming an aqueous solution of a water soluble, cross-linkable polysaccharide;</p> <p>(ii) initiating a first cross-linking reaction whereby cross-linking of said polysaccharide is effected using a polyfunctional cross-linking agent therefor;</p>	<p>RESTYLANE® Injectable Gel is a cross-linked biocompatible polysaccharide gel composition.</p> <p>RESTYLANE® Injectable Gel is manufactured by a process whereby hyaluronic acid prepared by fermentation of Streptococcus is first dissolved in an alkaline aqueous solution. Hyaluronic acid is a "a water soluble, cross-linkable polysaccharide."</p> <p>A cross-linking agent, 1,4-butanediol diglycidyl ether, is used to initiate a first cross-linking reaction. Thus, cross linking of the polysaccharide is effected using "a polyfunctional cross-linking agent." (See, e.g., column 4, lines 10-21 of U.S. Patent No. 5,827,937 for the</p>

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>(iii) sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide;  and</p> <p>(iv) performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel.</p>	<p>definition of polyfunctional cross-linking agent.)</p> <p>The above solution was first incubated and then diluted in a physiological buffer and neutralized. The dilution step accomplishes the step of "sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide," as recited in the claims. (See, e.g., column 3, lines 25-31 of U.S. Patent No. 5,827,937.)</p> <p>The activated polysaccharide was then rotary evaporated to form a viscoelastic gel with a neutral pH and a HA concentration of about 2% (w/w). The rotary evaporation step accomplishes the step of "performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel." (See, e.g., column 3, lines 32-56 of U.S. Patent No. 5,827,937.)</p> <p>Thus, Claim 1 reads on the method of manufacture for RESTYLANE® Injectable Gel.</p>
<p>2. A process according to claim 1, wherein the polysaccharide is selected</p>	<p>RESTYLANE® Injectable Gel comprises a cross-linked gel of hyaluronic acid.</p>

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
from the group consisting of glucose amino glucans.	Hyaluronic acid is a polysaccharide that is a "glucose amino glucan." Thus, Claim 2 reads on the method of manufacture for RESTYLANE® Injectable Gel.
3. A process according to claim 2, wherein said glucose amine glucan comprises hyaluronic acid.	RESTYLANE® Injectable Gel comprises a cross-linked gel of hyaluronic acid, which is a glucose amine glucan. Thus, Claim 3 reads on the method of manufacture for RESTYLANE® Injectable Gel.
5. A process according to claim 4, wherein said glycidyl ether comprises 1,4-butanediol diglycidylether.	RESTYLANE® Injectable Gel uses a glycidyl ether, which comprises 1,4-butanediol diglycidylether. Thus, Claim 5 reads on the method of manufacture for RESTYLANE® Injectable Gel.
6. A process according to claim 1, wherein said sterically hindering of the cross-linking reaction comprises diluting the aqueous medium in which the cross-linking reaction is performed, to accomplish a lower concentration of the polysaccharide in said medium.	As discussed above, the manufacture of RESTYLANE® Injectable Gel comprises a "cross-linking reaction" that includes "diluting the aqueous medium in which the cross-linking reaction is performed, to accomplish a lower concentration of the polysaccharide in said medium." Thus, Claim 6 reads on the method of manufacture for RESTYLANE® Injectable Gel.
7. A process according to claim 1, wherein said reintroduction of sterically unhindered conditions comprises evaporating the aqueous medium in which	The manufacture of RESTYLANE® Injectable Gel comprises a "reintroduction of sterically unhindered conditions" that includes "evaporating the aqueous

<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
the cross-linking reaction is performed, to accomplish a higher concentration of the polysaccharide in said medium.	medium in which the cross-linking reaction is performed, to accomplish a higher concentration of the polysaccharide in said medium." Thus, Claim 7 reads on the method of manufacture for RESTYLANE® Injectable Gel.
9. A process according to claim 1, wherein the initial cross-linking reaction in the presence of a polyfunctional cross-linking agent is performed at an alkaline pH, ether cross-linking reactions thereby being promoted.	The manufacture of RESTYLANE® Injectable Gel comprises an "initial cross-linking reaction in the presence of a polyfunctional cross-linking agent" that is "performed at an alkaline pH," with "ether cross-linking reactions thereby being promoted." Thus, Claim 9 reads on the method of manufacture for RESTYLANE® Injectable Gel.
10. The process of claim 9, wherein the cross-linking is effected at a pH above pH 9.	The manufacture of RESTYLANE® Injectable Gel comprises a "cross-linking" reaction that is "effected at a pH above pH 9." Thus, Claim 10 reads on the method of manufacture for RESTYLANE® Injectable Gel.
12. A process according to claim 1, wherein said sterical hindrance of the cross-linking reaction is accomplished before said cross-linking agent has been consumed.	The manufacture of RESTYLANE® Injectable Gel comprises a dilution step, which accomplishes "sterical hindrance of the cross-linking reaction." The dilution step is "accomplished before said cross-linking agent has been consumed." Thus, Claim 12 reads on the method of manufacture for RESTYLANE® Injectable Gel.
24. A cross-linked biocompatible	RESTYLANE® Injectable Gel is a cross-



<i>Claim as-issued</i>	<i>RESTYLANE® Injectable Gel</i>
<p>polysaccharide gel composition, which is obtainable by cross-linking of a cross-linkable polysaccharide with a polyfunctional cross-linking agent therefor in two steps,</p> <p>the first cross-linking step being terminated before gelation occurs by a sterical hindrance of the cross-linking reaction, and</p> <p>the second cross-linking step being initiated by reintroducing sterically unhindered conditions for said cross-linking reaction to continue the same up to a viscoelastic gel,</p>	<p>linked biocompatible polysaccharide gel composition, which is obtainable by cross-linking of a cross-linkable polysaccharide with a polyfunctional cross-linking agent in two steps.</p> <p>In a first step, a cross-linking agent, 1,4-butanediol diglycidyl ether, is used to initiate a first cross-linking reaction. The above solution is incubated and then diluted in a physiological buffer and neutralized. The dilution step accomplishes the step of "sterically hindering the first cross-linking reaction such that it is terminated before gelation occurs, resulting in the production of an activated polysaccharide," as recited in the claims. (See, e.g., column 3, lines 25-31 of U.S. Patent No. 5,827,937.)</p> <p>In a second step, the activated polysaccharide is then rotary evaporated to form a viscoelastic gel with a neutral pH and a HA concentration of about 2% (w/w). The rotary evaporation step accomplishes the step of "performing a second cross-linking reaction after sterically unhindered conditions are reintroduced for said activated polysaccharide to produce a viscoelastic gel." (See, e.g., column 3, lines 32-56 of U.S. Patent No. 5,827,937.)</p>

<i>Claim as-issued</i>	<i>RESTYLANE®Injectable Gel</i>
wherein said gel composition exhibits retained biocompatibility, viscoelasticity and does not swell substantially when placed in contact with water.	RESTYLANE® Injectable Gel exhibits retained biocompatibility, viscoelasticity and does not swell substantially when placed in contact with water.  Thus, Claim 24 reads on the method of manufacture for RESTYLANE® Injectable Gel.
33. A medical or prophylactic composition comprising a polysaccharide gel composition according to claim 24.	RESTYLANE® is a medical or prophylactic composition that comprises "a polysaccharide gel composition according to claim 24." Thus, Claim 33 reads on the method of manufacture for RESTYLANE® Injectable Gel.

**(10) RELEVANT DATES AND INFORMATION  
PURSUANT TO 35 U.S.C. § 156(g)**

The relevant dates and information pursuant to 35 U.S.C. § 156(g), and 37 C.F.R. § 1.740(a)(10)(v), to enable the Secretary of Health and Human Services to determine the applicable regulatory review period for a patent claiming a medical device are as follows:

- (a) *The effective date of the investigational device exemption (IDE) and the IDE number:* **IDE G990258** was submitted by Q-MED Scandinavia, Inc. on **October 14, 1999**, and became effective on **August 4, 2000**.
- (b) *The date on which the application for product approval or notice of completion of a product development protocol under section 515 of the Federal Food, Drug, and Cosmetic Act was initially submitted and the number of the application or protocol:* The application for product approval under section 515 of the Federal Food, Drug, and Cosmetic Act was initially submitted on **June 19, 2002**. The application number was **P020023**.
- (c) *The date on which the application was approved:* **December 12, 2003**.

**(11) BRIEF DESCRIPTION OF SIGNIFICANT ACTIVITIES**

The following is a brief description of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to RESTYLANE® Injectable Gel and the significant dates applicable to such activities.

Date	To	From	Type	Summary
March 17, 1999	FDA	Akin, Gump	Submission	Meeting request Letter Pre-IDE Meeting
October 14, 1999	FDA	A/G	Submission	Filed original IDE for treatment of cutaneous contour deformities such as nasolabial folds.
November 12, 1999	A/G	FDA	Facsimile	FDA granted conditional approval for two sites with 10 subjects each. FDA stated that issues of clinical design remain that must be addressed. Letter lists deficiencies and the protocol and RPI must be revised.
December 3, 1999	FDA	A/G	Letter	Requested a meeting with FDA to discuss clinical issues
December 15, 1999			Minutes	Safety, study design, hypersensitivity and other issues were addressed. From the minutes it appears that a formal meeting was set for January 11, 2000.
December 28, 1999				First screening visit; patient examined and received collagen test in the arm
January 6, 2000	FDA	A/G	Submission	Submission of safety data in response to questions raised in FDA's November 12, 1999 letter. This letter also refers to the December 15, 1999 conference call.
January 11, 2000			Minutes	Safety and clinical issues were discussed. FDA expects a revised protocol and

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Date	To	From	Type	Summary
				invited further teleconferences.
February 4, 2000	A/G	FDA	Letter	FDA acknowledged the January 6, 2000 submission and conditionally approved the IDE for 45 days but still for only 2 sites and 10 patients each. The deficiencies from the November 12, 1999 letter must be corrected.
March 16, 2000				First Patient included and treated within the study
March 16, 2000	FDA	A/G	Submission	Filed responses to FDA's November 12, 1999 letter and submitted a revised protocol (31 GE 0003) and CRF.
April 13, 2000	A/G	FDA	Letter	FDA acknowledged the March 16, 2000 submission but still only granted conditional approval. The protocol was still considered unacceptable.
April 26, 2000			Minutes	Teleconference minutes cover various protocol issues including duration, touch-up, validation of clinical endpoints, statistics, informed consent, etc.
May 11, 2000			Minutes	Teleconference
May 26, 2000	FDA	A/G	Submission	Provided FDA with revised protocol, the minutes of the May 11, 2000 teleconference, and specific responses to deficiencies.
June 9, 2000	FDA	A/G	Submission	Provided FDA with copies of various CRFs.
June 29, 2000	A/G	FDA	Letter	FDA acknowledged receipt of submissions dated May 26 and June 9 2000. Letter states the application remains conditionally approved and limited to 5 sites and 30 subjects. At issue is the validity of the clinical endpoints. FDA expects a revised protocol.

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Date	To	From	Type	Summary
July 6, 2000			Minutes	Minutes of a teleconference with FDA covering the June 29, 2000 letter. Call covered statistical issues.
July 7, 2000			Minutes	Minutes of a teleconference with FDA covering the June 29, 2000 letter. Call covered not statistical issues.
July 11, 2000	FDA	Buchanan Ingersoll (BI)	Submission	Submitted revised protocol, patient diaries, CRFs, example photographs in response to FDA's June 29, 2000 letter.
August 4, 2000	BI	FDA	Letter	FDA approved the IDE. FDA provided two points of advice regarding the analysis of data for safety and effectiveness.
October 12, 2000	FDA	BI	Letter	Requested that FDA allow the addition of another clinical site.
November 3, 2000	BI	FDA	Letter	FDA allowed the addition of one more clinical site.
November 14, 2000	FDA	BI	Submission	Covers manufacturing changes: scale up from 4000 to 15, 000 syringes; removed methanol from process; changed test methods and added bioburden.
December 11, 2000	BI	FDA	Letter	FDA acknowledged the November 14, 2000 letter. FDA accepted the manufacturing changes submitted.
December 12, 2000	FDA	BI	Submission	Submitted "Validation of the Wrinkle Severity Rating Scale – A Sub-study within 31 GE 0003.
January 12, 2001	BI	FDA	Letter	Submission of December 12, 2000 unacceptable. Submission only covers a 2-point scale while the protocol requires a 5-point scale. FDA requested data within 45 days of date of the letter.
January 31, 2001	FDA	BI	Fax	Sent FDA a copy of the July 6, 2000 teleconference minutes.

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Date	To	From	Type	Summary
February 26, 2001	FDA	BI	Submission	Submitted revised clinical validation report – see December 12, 2000 and January 12, 2001.
March 22, 2001	BI	FDA	Letter	FDA acknowledged submission of February 26, 2001. FDA accepted the revised validation report.
June 19, 2002	FDA	Q-MED	Submission	Submitted original PMA for the treatment of cutaneous contour deformities such as nasolabial folds. Also informed FDA facility ready for inspection in August 2002.
July 30, 2002	Q-MED	FDA	Letter	FDA made a threshold determination that the PMA is sufficiently complete to permit substantive review and suitable for filing. Deficiencies were noted in the letter.
September 6, 2002	FDA	Q-MED	Submission	Provided a partial response to FDA is issues listed in the July 30, 2002 FDA letter. Responds to 3 of 7 deficiencies including clinical, manufacturing, statistical areas.
September 12, 2002	FDA	Q-MED	Submission	Provided financial disclosure in and also informed FDA that some labeling would be modified per FDA's request (July 30, 2002 letter).
October 4, 2002	Q-MED	FDA	Letter	FDA scheduled a meeting for October 10, 2002; this was a 100-day meeting to discuss deficiencies in the PMA. FDA listed the current deficiencies in the application.
November 18, 2002	Q-MED	FDA	Letter	FDA stated PMA lacks information to complete review. This 10-page letter lists the deficiencies found by FDA.
December 27, 2002	FDA	Q-MED	Submission	Provided a complete response to FDA's November 18, 2002 letter. Some

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Date	To	From	Type	Summary
				additional information was included as well to update the PMA. Also, provided comments regarding the need for a Panel meeting.
May 5, 2003	Q-MED	FDA	Letter	Received a deficiency letter from FDA.
June 16, 2003	FDA	Q-MED	Submission	Provided a complete response to the FDA deficiency letter of May 5, 2003. Provided data for risk assessment for residual BDDE, adverse events for other countries, safety data on specific ethnic groups.
Aug 8, 2003	FDA	Q-MED	Letter	Notified FDA that the letter represents the final report for the IDE and stated that the final report was submitted in the PMA. No further clinical trials are anticipated.
November 21, 2003				Advisory Panel meeting
December 12, 2003	Q-MED	FDA	Approval Letter	FDA approved the PMA for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. There was agreement to perform a Phase IV study.



**PLEASE NOTE:** IDE G990258 was submitted by Q-MED Scandanavia on October 14, 1999 and became effective on August 4, 2000. P020023 was submitted by Q-MED Scandinavia, Inc. on June 19, 2002, and approved by the FDA on December 12, 2003. Q-MED Scandinavia, Inc. is a wholly owned subsidiary of Q-MED AB. An authorization from Q-MED Scandinavia, Inc. to Q-MED AB, to rely upon the activities of Q-MED Scandinavia, Inc. before the FDA during the regulatory review period in making its applications for extension and extension of patent term, and granting the Commissioner for Patents and the Secretary for Health and Human Services and/or Commissioner of Food and Drugs the right to refer to IDE G990258 and P020023 in determining the eligibility of Q-MED AB for such extensions, is attached as ATTACHMENT G.

**(12) ELIGIBILITY FOR EXTENSION OF PATENT TERM**

In the opinion of Q-MED AB, U.S. Patent No. 5,827,937 is eligible for the requested extension of patent term, and the length of extension claimed is **879 days**.

The length of extension of the term of U.S. Patent No. 5,827,937 of **879 days** is based upon 37 C.F.R. §1.777, which states that the term of the patent for a medical device will be extended by the length of the regulatory review period for the product as determined by the Secretary of Health and Human Services, reduced as appropriate pursuant to paragraphs (d)(1) through (d)(6) of this section.

**37 C.F.R. §1.777(c)**

First of all, the length of the regulatory review period for a medical device will be determined by the Secretary of Health and Human Services. Under 35 U.S.C. 156(g)(3)(B), it is the sum of:

- (1) The number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act; and
- (2) The number of days in the period beginning on the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act, and ending on the date such application was approved

under such Act or the period beginning on the date a notice of completion of a product development protocol was initially submitted under section 515(f)(5) of the Act and ending on the date the protocol was declared completed under section 515(f)(6) of the Act.

37 C.F.R. §1.777(c)(1)

With respect to 37 C.F.R. §1.777(c)(1), the date a clinical investigation on humans involving the device was begun was **December 28, 1999**. The date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act was **June 19, 2002**.

Thus, the "number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act" is the number of days between **December 28, 1999** and **June 19, 2002**, which is **904 days**.

37 C.F.R. §1.777(c)(2)

With respect to 37 C.F.R. §1.777(c)(2), the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act was **June 19, 2002**. The date such application was approved under such Act was **December 12, 2003**.

Thus, the number of days in “the period beginning on the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act, and ending on the date such application was approved under such Act” is the number of days between June 19, 2002 and December 12, 2003, which is 541 days.

Thus, the sum of the periods in 37 C.F.R. §1.777(c)(1) and 37 C.F.R. §1.777(c)(2) is equal to 904+541, which is 1445 days.

37 C.F.R. §1.777(d)

Next, the regulatory review period for the product, as determined by the Secretary of Health and Human Services, is reduced as appropriate pursuant to paragraphs (d)(1) through (d)(6) of 37 C.F.R. §1.777(d). At the outset, we note that 37 C.F.R. §1.777(d)(6) is not applicable, since U.S. Patent No. 5,827,937 was not “issued before September 24, 1984.”

37 C.F.R. §§1.777(d)(1)-(5) state that:

The term of the patent as extended for a medical device will be determined by --

(1) Subtracting from the number of days determined by the Secretary of Health and Human Services to be in the regulatory review period pursuant to paragraph (c) of this section:

(i) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section which were on and before the date on which the patent issued;

(ii) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section during which it is determined under 35 U.S.C. 156(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence;

(iii) One-half the number of days remaining in the period defined by paragraph (c)(1) of this section after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii) of this section; half days will be ignored for purposes of subtraction;

(2) By adding the number of days determined in paragraph (d)(1) of this section to the original term of the patent as shortened by any terminal disclaimer;

(3) By adding 14 years to the date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act or the date a product development protocol was declared completed under section 515(f)(6) of the Act;

(4) By comparing the dates for the ends of the periods obtained pursuant to paragraphs (d)(2) and (d)(3) of this section with each other and selecting the earlier date;

(5) If the original patent was issued after September 24, 1984,

(i) By adding 5 years to the original expiration date of the patent or earlier date set by terminal disclaimer; and

(ii) By comparing the dates obtained pursuant to paragraphs (d)(4) and (d)(5)(i) of this section with each other and selecting the earlier date;

37 C.F.R. §1.777(d)(1)

The periods in paragraph d(1) are calculated as follows:

(i) The number of days in the periods of paragraphs (c)(1) and (c)(2) of this section which were on and before the date on which the patent issued would be zero.

(In this regard, the patent issued on **October 27, 1998**. The clinical investigation on humans involving the device did not begin until **December 28, 1999** and the application under section 515 of the Federal Food, Drug, and Cosmetic Act was not submitted until **June 19, 2002**.)

(ii) In the Applicant's opinion, marketing applicant acted with due diligence as defined at 35 U.S.C. §156(d)(3) during the above calculated periods of paragraphs (c) (1) and (c)(2).

Thus, **zero days** are subtracted from the regulatory review period.

(iii) As mentioned above, the number of days calculated according to paragraphs (d)(1)(i) and (ii) of this section are both zero. Thus, "one-half the number of days remaining in the period defined by paragraph (c)(1) after that period is reduced in accordance with paragraphs (d)(1)(i) and (ii) of this section" would be  $=(904-0)/2$ , or **452 days**.

Thus, subtracting from the number of days determined by the Secretary of Health and Human Services to be in the regulatory review period pursuant to paragraph (c) of this section would result in 1445-452 days, which is **993 days**.

37 C.F.R. §1.777(d)(2)

The number of days determined in paragraph (d)(1) of this section would be **993 days**, as described in detail above.

The original term of the patent as shortened by any terminal disclaimer would be 20 years from issue, *i.e.*, **July 17, 2015**.

Thus, adding the number of days determined in paragraph (d)(1) of this section to the original term of the patent as shortened by any terminal disclaimer would be:

= 993 days + July 17, 2015

= **April 5, 2018**

37 C.F.R. §1.777(d)(3)

The date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act was December 12, 2003.

Thus, adding 14 years to the date of approval of the application under section 515 of the Federal Food, Drug, and Cosmetic Act would be:

= December 12, 2003 + 14 years

= **December 12, 2017.**

37 C.F.R. §1.777(d)(4)

The dates for the ends of the periods obtained pursuant to paragraphs (d)(2) and (d)(3) of this section are **April 5, 2018** and **December 12, 2017** respectively.

Of these two dates, the earlier date is **December 12, 2017.**

37 C.F.R. §1.777(d)(5)

(i) The original expiration date of the patent would be July 17, 2015. Adding 5 years to the original expiration date of the patent or earlier date set by terminal disclaimer would result in a date of July 17, 2015 + 5 years, *i.e.*, **July 17, 2020.**



(ii) The dates obtained pursuant to paragraphs (d)(4) and (d)(5)(i) of this section are  
**December 12, 2017 and July 17, 2020** respectively.

Of these two dates, the earlier date is **December 12, 2017**.

**(13) DUTY OF DISCLOSURE**

Q-MED AB acknowledges a duty to disclose to the Director of the U.S. Patent & Trademark Office and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought herein.

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**(14) FEES**

The Director is hereby authorized to charge the amount of \$ 1,120 (37 C.F.R. § 1.20(j)(1)) to Deposit Account No. 02-4800 for receiving and acting upon the application for extension.

The Director is hereby also authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

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**(15) NAME AND ADDRESS FOR CORRESPONDENCE**

Please address all inquiries and correspondence relating to this application for patent  
extension to:

Benton S. Duffett  
BURNS, DOANE, SWECKER & MATHIS, L.L.P.  
P.O. Box 1404  
Alexandria, Virginia 22313-1404  
Telephone: (703) 836-6620  
Facsimile: (703) 836-2021

**(16) MULTIPLE COPIES**

This application for extension, together with the appended ATTACHMENTS A through H, is being submitted in original form along with three copies. The undersigned hereby certifies that the copies of this application for extension, together with the appended ATTACHMENTS A through H, filed herewith are true and correct copies.

**(17) DECLARATION**

I, Benton S. Duffett (the undersigned duly authorized agent for Q-MED AB) do hereby declare as follows:

(a) I am a patent attorney authorized to practice before the U.S. Patent & Trademark Office and am authorized to represent Q-MED AB in this application for patent term extension by virtue of a Power of Attorney executed on August 19, 1997 (a copy of the Power of Attorney is attached hereto as ATTACHMENT H);

(b) I have reviewed and understand the contents of this application for patent term extension;

(c) I believe that U.S. Patent No. 5,827,937 is subject to patent term extension pursuant to 35 U.S.C. § 156 and 37 C.F.R. §§ 1.710, 720, 740 and 777;

(d) I believe that an extension of the length claimed is justified under 35 U.S.C. § 156 and the applicable regulations; and

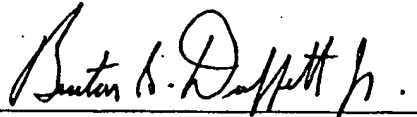
(e) I believe that U.S. Patent No. 5,827,937 meets the conditions for extension of the term of a patent set forth in 37 C.F.R. § 1.720.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application being submitted herewith or any extension of patent term granted thereon.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By:



Benton S. Duffett, Jr.  
Registration No. 22,030

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

Date: February 10, 2004



UNITED STATES PATENT AND TRADEMARK OFFICE

JUN 7 2004

#19  
Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Office of Regulatory Policy  
HFD - 13  
5600 Fishers Lane  
Rockville, MD 20857

Attention: Claudia Grillo

The attached application for patent term extension of U.S. Patent No. 5,827,937 was filed on February 10, 2004, under 35 U.S.C. § 156.

The assistance of your Office is requested in confirming that the product identified in the application has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved. Since a determination has not been made whether the patent in question claims a product which has been subject to the Federal Food, Drug and Cosmetic Act, or a method of manufacturing or use of such a product, this communication is NOT to be considered as notice which may be made in the future pursuant to 35 U.S.C. § 156(d)(2)(A).

Our review of the application to date indicates that the subject patent would be eligible for extension of the patent term under 35 U.S.C. § 156.

Inquiries regarding this communication should be directed to the undersigned at (703) 306-3159 (telephone) or (703)872-9411 (facsimile).

Karin Ferriter  
Senior Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Commissioner  
for Patent Examination Policy

cc: Benton S. Duffett  
Burns, Doane, Swecker & Mathis, LLP  
PO Box 1404  
Alexandria VA 22313-1404





DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Rockville MD 20857

FEB 24 2004

Re: Restylane  
Docket No. 2004E-0308

The Honorable Jon Dudas  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office  
Box Pat. Ext.  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Director Dudas:

This is in regard to the application for patent term extension for U.S. Patent No. 5,827,937 filed by Q-Med AB under 35 U.S.C. § 156. The medical device claimed by the patent is Restylane, which was assigned PMA No. P020023.

A review of the Food and Drug Administration's official records indicates that this product was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). Our records also indicate that it represents the first permitted commercial marketing or use of the product, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in *Glaxo Operations UK Ltd. v. Quigg*, 706 F. Supp. 1224 (E.D. Va. 1989), *aff'd*, 894 F. 2d 392 (Fed. Cir. 1990).

The PMA was approved on December 12, 2003, which makes the submission of the patent term extension application on February 10, 2004, timely within the meaning of 35 U.S.C. § 156(d)(1).

Should you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the *Federal Register*, and notify you of our determination.

Please let me know if we can be of further assistance.

Sincerely yours,

Jane A. Axelrad  
Associate Director for Policy  
Center for Drug Evaluation and Research

cc: Bennet S. Duffet  
Burns, Doane, Swecker, & Mathis, L.L.P.  
P.O. Box 1404  
Alexandria, VA 22313-1404



APR - 4 2007

Benton S. Duffett  
Burns, Doane, Swecker & Mathis, LLP  
P.O. Box 1404  
Alexandria VA 22313-1404In re: Patent Term Extension  
Application for  
U.S. Patent No. 5,827,937

## NOTICE OF FINAL DETERMINATION

A determination has been made that U.S. Patent No. 5,827,937, which claims the medical device RESTYLANE® (Injectable Gel), is eligible for patent term extension under 35 U.S.C. § 156. The period of extension has been determined to be 879 days.

A single request for reconsideration of this final determination as to the length of extension of the term of the patent may be made if filed within one month of the date of this notice. Extensions of time under 37 CFR § 1.136(a) are not applicable to this time period. In the absence of such request for reconsideration, the Director will issue a certificate of extension, under seal, for a period of 879 days.

The period of extension has been calculated using the Food and Drug Administration determination of the length of the regulatory review period published in the Federal Register of June 13, 2006 (71 Fed. Reg. 34138). Under 35 U.S.C. § 156(c):

$$\begin{aligned}\text{Period of Extension} &= \frac{1}{2} (\text{Testing Phase}) + \text{Approval Phase} \\ &= \frac{1}{2} (949) + 542 \\ &= 1016 \text{ days (2.8 years)}\end{aligned}$$

Since the regulatory review period began November 14, 1999, after the patent issued (October 27, 1998), the entire regulatory review period has been considered in the above determination of the length of the extension period 35 U.S.C. § 156(c). No determination of a lack of due diligence under 35 U.S.C. § 156(c)(1) was made.

However, the 14 year exception of 35 U.S.C. § 156(c)(3) operates to limit the term of the extension in the present situation because it provides that the period remaining in the term of the patent measured from the date of approval of the approved product plus any patent term extension cannot exceed fourteen years. The period of extension calculated above, 1016 days, would extend the patent from July 17, 2015 to April 18, 2018, which is beyond the 14-year limit (the approval date is December 12, 2003, thus the 14 year limit is December 12, 2017). The period of extension is thus limited to 879 days, by operation of 35 U.S.C. § 156(c)(3). Accordingly, the period of extension is the number of days to extend the term of the patent from its original expiration date, July 17, 2015, to and including December 12, 2017, or 879 days.

The limitations of 35 U.S.C. 156(g)(6) do not operate to further reduce the period of extension determined above.

Upon issuance of the certificate of extension, the following information will be published in the Official Gazette:

U.S. Patent No.: 5,827,937

Granted:	October 27, 1998
Original Expiration Date <sup>1</sup> :	July 17, 2015
Applicant:	Bengt Ågerup
Owner of Record:	Q-Med AB
Title:	Polysaccharide Gel Composition
Product Trade Name:	RESTYLANE®
Term Extended:	879 days
Expiration Date of Extension:	December 12, 2017

Any correspondence with respect to this matter should be addressed as follows:

By mail:	Mail Stop Patent Ext. Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450.	By FAX:	(571) 273-7754
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Telephone inquiries related to this determination should be directed to the undersigned at (571) 272-7754.



Kathleen Kahler Fonda  
Legal Advisor  
Office of Patent Legal Administration  
Office of the Deputy Assistant Commissioner  
for Patent Policy and Projects

cc:	Office of Regulatory Policy HFD - 7 5600 Fishers Lane Rockwall II Rm. 110 Rockville, MD 20857	Re:	RESTYLANE® (Injectable Gel)
	Attention: Beverly Friedman		FDA Docket No. 2004E-0308

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<sup>1</sup>Subject to the provisions of 35 U.S.C. § 41(b).

# UNITED STATES PATENT AND TRADEMARK OFFICE

## (12) CERTIFICATE EXTENDING PATENT TERM UNDER 35 U.S.C. § 156

(68) PATENT NO. : 5,827,937  
(45) ISSUED : October 27, 1998  
(75) INVENTOR : Bengt Ågerup  
(73) PATENT OWNER : Q-Med AB  
(95) PRODUCT : RESTYLANE® (Injectable Gel)

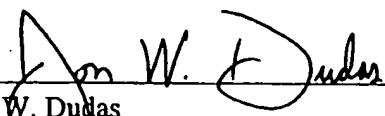
This is to certify that an application under 35 U.S.C. § 156 has been filed in the United States Patent and Trademark Office, requesting extension of the term of U.S. Patent No. 5,827,937 based upon the regulatory review of the product RESTYLANE® (Injectable Gel) by the Food and Drug Administration. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

(94) 879 days

from July 17, 2015, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).



I have caused the seal of the United States Patent and Trademark Office to be affixed this 4th day of October 2007.

  
Jon W. Dudas  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office